the ability of the polypeptides   preferred embodiment of the	 antibodies and agonists or for inhibiting endothelial cell	n) to	inhibit caspase protease- embodiment of the invention	mediated apoptosis. includes a method for	Exemplary assays for caspase stimulating endothelial cell	apoptosis that may be used or proliferation. An alternative	routinely modified to test highly preferred embodiment	 polypeptides of the invention method for inhibiting	(including antibodies and endothelial cell proliferation.	agonists or antagonists of the A highly preferred	 disclosed in Romeo et al., includes a method for	Cardiovasc Res 45(3): 788-794   stimulating endothelial cell	 Pharmacol 127(7): 1633-1640 preferred embodiment of the	(1999); and J Atheroscler invention includes a method	Thromb 3(2): 75-80 (1996); for inhibiting endothelial cell	ich	are herein incorporated by embodiment of the invention	reference in its entirety.	Endothelial cells that may be stimulating apoptosis of	used according to these assays endothelial cells. An	are publicly available (e.g., alternative highly preferred	through commercial sources).   embodiment of the invention	Exemplary endothelial cells includes a method for	that may be used according to inhibiting (e.g., decreasing)	these assays include hovine apportosis of endothelial cells	_
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embodiment of the invention includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial
(bAEC), which are an example of endothelial cells which line	blood vessels and are involved	in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																							
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infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous). glomus tumors.	(

peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury	such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal	diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph	angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred
pe an in principle w	C It is a Q. S. S.	d a o gg ii. A th	a d d d d d d d d d d d d d d d d d d d

indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").	Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis,
		Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1
		Production of ICAM-1
		1278
-		HMDAQ29
		330

Stroke, and Asthma.					·	Preferred indications include	blood disorders (e.g., as described below under	"Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"), and infection (e.g., an
expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays	disclosed in: Kolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et	al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154- L1163 (2000), the contents of each of which is herein	incorporated by reference in its entirety. Cells that may be used according to these assays	are publicly available (e.g., through the ATCC) and/or may be routinely generated.	Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as	bovine AOSMC. Assays for the activation of	transcription through the cAMP response element are	well-known in the art and may be used or routinely modified	to assess the ability of polypeptides of the invention
						Activation of	transcription through cAMP	response element in immune cells (such	as T-cells).
						1278	2		
						HMDA020			
							330		

infectious disease as described below under "Infectious Disease"). Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described below), immunodeficiencies (e.g., as described below),	boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional	preferred indications include inflammation and	inflammatory disorders. Highly preferred indications	include neoplastic diseases (e.g., leukemia, lymphoma,	and/or as described below under "Hypermroliferative	Disorders"). Highly preferred	and cancers, such as, for	example, leukemia, lymphoma (e.g., T cell lymphoma.	Burkitt's lymphoma, non-	Hodgkins lymphoma,	Hodgkin''s disease), melanoma and prostate
(including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB	transcription factors, and modulate expression of genes involved in a wide variety of	cell functions. Exemplary assays for transcription through the cAMP response	element that may be used or routinely modified to test	cAMP-response element activity of polypeptides of the	invention (including antibodies and agonists or antagonists of	the invention) include assays disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and Malm, Methods in Enzymol	216:362-368 (1992); Henthorn et al. Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	a, virus Genes 13(2):103-117 (1997); and Belkowski et al., J	Immunol 161(2):659-665 (1998), the contents of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used

breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia,	acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,	suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative
publicly available (e.g., through the ATCC).  Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is a suspension	culture of IL-2 dependent cytotoxic T cells.			Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or
		·	J	Activation of transcription through serum response element in immune cells (such
				1279
				HMEA148
				331

preferred embodiment of the invention includes a method for stimulating (e.g.,	increasing) TNF alpha production. Preferred	indications include blood	disorders (e.g., as described below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Linhly preferred indications
routinely modified to assess the ability of polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) to	regulate the serum response	factors and modulate the	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	milion on oldelions
as T-cells).																•							· · · · · · · · · · · · · · · · · · ·			

eases	noma,	low	utive	nally,	ations		xample,	•	g;	pild	breast,	-	brain,	er. Other	include		plastic	ır		splasia.	include		ytopenia,	ute	(ALL),	iple	mphoma,	lomatous	y bowel	
include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	diagonal months
include	(e.g., le	and/or	under "	Disord	highly	include	cancers	leukem	melano	malign	tumors	lung, c	esopha	liver ar	preferr	benign	disorde	conditi	examp	metapl	Prefer	anemia	leukop	Hodgk	lymph	plasma	myelo	arthriti	disease	4:0000
through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.																							
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neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cellmediate humoral or proteins evaluate the production of
	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1279
	HMEA148
	331

cytokines, such as RANTES.	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells
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	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammatory disorders. An additional highly preferred
(HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention
	Activation of transcription through NFAT response element in immune cells (such as T-cells).
	1280
	HMECK83
	332

l llation, arditis, se,	asing) ernative iment is a s.g., on. A tion is ncement Highly clude s lood- lood- lers"), ers"),
Soriasis, f immune ansplante sues, ypercoagu tus, endocyme Dises lergy.	erred  of the inve thod for  e.g., incre on. An alt ed embod on include hibiting (  fo producti red indica n or enha nmunity.  cations in rs (e.g., a ow under ivity", "B ders", and lar Disord (e.g., as ow under ivity", "B icers", and lar Disord (e.g., as)
neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing)  IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g.,
neu suț rea cor E or E dia dia ast	10.0
	6 is produced strong 3. IL-6 4.4 induced and increases lgA plays a mmunity). 5. o autoimmun ytomas, hronic 6 diseases. 6 diseases. 7 momodulator 7 a by a large where the is strongly okines, growth onnes are wel and may be and may be and may be of the strongly okines, growth onnes are wel and may be of the strongly okines, growth onnes are wel and may be of the strongly okines, growth on the strongly of t
	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to
	LL-  LIGH  BAS  BAS  BAS  BAS  BAS  BAS  BAS  BA
	Production of IL-6
	1281
	HMEET96
	333

	     		polypeptides of the invention	rheumatoid arthritis, systemic
			(including antibodies and	lupus erythematosis, multiple
	-		agonists or antagonists of the	sclerosis and/or as described
			invention) to mediate	below) and
			immunomodulation and	immunodeficiencies (e.g., as
			differentiation and modulate T	described below). Highly
			cell proliferation and function.	preferred indications also
			Exemplary assays that test for	include boosting a B cell-
			immunomodulatory proteins	mediated immune response
			evaluate the production of	and alternatively suppressing a
			cytokines, such as IL-6, and	B cell-mediated immune
			the stimulation and	response. Highly preferred
			upregulation of T cell	indications include
			proliferation and functional	inflammation and
			activities. Such assays that	inflammatory
			may be used or routinely	disorders.Additional highly
-			modified to test	preferred indications include
			immunomodulatory and	asthma and allergy. Highly
			diffferentiation activity of	preferred indications include
			polypeptides of the invention	neoplastic diseases (e.g.,
P No.			(including antibodies and	myeloma, plasmacytoma,
			agonists or antagonists of the	leukemia, lymphoma,
			invention) include assays	melanoma, and/or as described
-			disclosed in Miraglia et al., J	below under
			Biomolecular Screening 4:193-	"Hyperproliferative
			204(1999); Rowland et al.,	Disorders"). Highly preferred
			"Lymphocytes: a practical	indications include neoplasms
			approach" Chapter 6:138-160	and cancers, such as, myeloma,
		-	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
			Immunol 158:2919-2925	lymphoma, melanoma, and
			(1997), the contents of each of	prostate, breast, lung, colon,

			which are herein incorporated	pancreatic, esophageal,
			by reference in its entirety.	stomach, brain, liver and
			Human dendritic cells that may	urinary cancer. Other preferred
			be used according to these	indications include benign
			assays may be isolated using	dysproliferative disorders and
			techniques disclosed herein or	pre-neoplastic conditions, such
			otherwise known in the art.	as, for example, hyperplasia,
			Human dendritic cells are	metaplasia, and/or dysplasia.
			antigen presenting cells in	Preferred indications include
			suspension culture, which,	anemia, pancytopenia,
			when activated by antigen	leukopenia, thrombocytopenia,
			and/or cytokines, initiate and	Hodgkin's disease, acute
			upregulate T cell proliferation	lymphocytic anemia (ALL),
			and functional activities.	multiple myeloma, Burkitt's
				lymphoma, arthritis, AIDS,
				granulomatous disease,
				inflammatory bowel disease,
				sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
 				reactions to transplanted
 ,				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, and Lyme Disease.
				An additonal preferred
				indication is infection (e.g., an
				infectious disease as described
				below under "Infectious
				Disease").
HMEET96	1281	Inhibition of	Reporter Assay: construct	

	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and
ng its its al., the its	Endothelial cells, which are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary endothelial cells that may be used in ICAM production assays include human umbilical vein
squalene synthetase gene transcription.	Production of ICAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1281
	HMEET96
333	333

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cardiovascular disorders (such	as described below under	"Immune Activity", "Blood-	Related Disorders",	"Hyperproliferative Disorders"	and/or "Cardiovascular	Disorders"). Highly preferred	indications include neoplasms	and cancers such as, for	example, leukemia, lymphoma,	melanoma, renal cell	carcinoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.										
endothelial cells (HUVEC),	and are available Iroin	commercial sources. The	expression of ICAM (CD54),a	intergral membrane protein,	can be upregulated by	cytokines or other factors, and	ICAM expression is important	in mediating immune and	endothelial cell interactions	leading to immune and	inflammatory responses.	Assays for measuring	expression of ICAM-1 are	well-known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate ICAM-1	expression. Exemplary assays	that may be used or routinely	modified to measure ICAM-1	expression include assays	disclosed in: Rolfe BE, et al.,	Atherosclerosis, 149(1):99-110	(2000); Panettieri RA Jr, et al.,	J Immunol, 154(5):2358-2365	(1995); and, Grunstein MM, et	al., Am J Physiol Lung Cell
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. 8	Highly preferred indications include asthma, allergy, ation, hypersensitivity reactions, inflammation, and inflammatory disorders.  Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting or inhibiting immune cell proliferation.  Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under and/or as described below under
Mol Physiol, 278(6):L1154- L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety.	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem
	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
	1282
	HMIAL37
	334

Disorders"). Highly preferred	indications include boosting an	eosinophil-mediated immune	response, and suppressing an	eosinophil-mediated immune	response.	•																								
Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and
			,																											
		-																												

			activation of c-Jun NH2-	Francis .
			terminal kinase and p38	
			mitogen-activated protein	
			kinase in human eosinophils"	
			Clin Exp Immunol;	
			Oct;122(1):20-7 (2000);	
			Hebestreit H, et al.,	
			"Disruption of fas receptor	
			signaling by nitric oxide in	
			eosinophils" J Exp Med; Feb	
			2;187(3):415-25 (1998); J	
			Allergy Clin Immunol 1999	
			Sep;104(3 Pt 1):565-74; and,	
			Sousa AR, et al., "In vivo	
			resistance to corticosteroids in	
			bronchial asthma is associated	
			with enhanced	
			phosyphorylation of JUN N-	
			terminal kinase and failure of	
			prednisolone to inhibit JUN N-	
			terminal kinase	
			phosphorylation" J Allergy	
			Clin Immunol; Sep;104(3 Pt	
			1):565-74 (1999); the contents	
			of each of which are herein	
			incorporated by reference in its	
			entirety.	dution in
HMIAL37	1282	Production of IL-10	Assays for production of IL-10	Highly preferred indications
		and activation of T-	and activation of T-cells are	include allergy and asthma.
		cells.	well known in the art and may	Additional highly preferred
			be used or routinely modified	indications include immune
	Lincoln			

and hematopoietic disorders (e.g., as described below under	'Immune Activity", and 'Blood-Related Disorders"),	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, Crohn"s	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response.																
tion	(including antibodies and "Im agonists or antagonists of the "Ble		inhibit production of IL-10   rheu	and/or activation of T-cells.   lupu	Exemplary assays that may be   dise	used or routinely modified to and		polypeptides and antibodies of   desc	the invention (including cell.			production and/or T-cell resp	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be	used according to these assays
to po	(ir ag	o ii	lai	an	<u> </u>	sn	ass	od	the	ag	ni	ud	nd	ex	dis dis	Rc		Br		he	the the			03	he	ea lea	<u> </u>	sn

y be are e e	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly odies preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the immunomodulation, induce
	Production of MCP-1
	1283
	HMIAP86
	335

chemotaxis, and modulate	Additional highly preferred
 immune cell activation.	indications include
Exemplary assays that test for	inflammation and
immunomodulatory proteins	inflammatory disorders.
evaluate the production of cell	Preferred indications include
surface markers, such as	blood disorders (e.g., as
 monocyte chemoattractant	described below under
protein (MCP), and the	"Immune Activity", "Blood-
activation of monocytes and T	Related Disorders", and/or
cells. Such assays that may be	"Cardiovascular Disorders").
 used or routinely modified to	Highly preferred indications
test immunomodulatory and	include autoimmune diseases
diffferentiation activity of	(e.g., rheumatoid arthritis,
polypeptides of the invention	systemic lupus erythematosis,
(including antibodies and	multiple sclerosis and/or as
 agonists or antagonists of the	described below) and
invention) include assays	immunodeficiencies (e.g., as
 disclosed in Miraglia et al., J	described below). Preferred
Biomolecular Screening 4:193-	indications also include
204(1999); Rowland et al.,	anemia, pancytopenia,
"Lymphocytes: a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	lymphocytic anemia (ALL),
Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
 Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
158:2919-2925 (1997), the	disease, inflammatory bowel
contents of each of which are	disease, sepsis, neutropenia,
herein incorporated by	neutrophilia, psoriasis,
reference in its entirety.	suppression of immune
Human dendritic cells that may	reactions to transplanted

ng n or	AND TO THE PROPERTY OF THE PRO				be used according to these	organs and tissues,
techniques disclosed herein or otherwise known in the art.  Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and or cytokines, initiate and upregulate T cell proliferation and functional activities.  HMIAP86 1283 Production of MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chenotaxis are well known in the art and may be					assavs may be isolated using	hemophilia, hypercoagulation,
otherwise known in the art.  Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.  HMIAP86 1283 Production of MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be					techniques disclosed herein or	diabetes mellitus, endocarditis,
Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.  HMIAP86 1283 Production of MIP-lalpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be					otherwise known in the art.	meningitis (bacterial and
antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.  HMIAP86 1283 Production of MIP-lalpha FMAT. Assays MIP lalpha for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be					Human dendritic cells are	viral), Lyme Disease, asthma,
suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.  HMIAP86 1283 Production of MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be					antigen presenting cells in	and allergy Preferred
when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.  HMIAP86 1283 Production of MP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be					suspension culture, which,	indications also include
and/or cytokines, initiate and upregulate T cell proliferation and functional activities.  HMIAP86 1283 Production of MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be					when activated by antigen	neoplastic diseases (e.g.,
upregulate T cell proliferation and functional activities.  HMIAP86 1283 Production of for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be					and/or cytokines, initiate and	leukemia, lymphoma, and/or as
AMIAP86 1283 Production of for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be					upregulate T cell proliferation	described below under
HMIAP86 1283 Production of MIP-1alpha FMAT. Assays MIP lalpha for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be					and functional activities.	"Hyperproliferative
HMIAP86 1283 Production of for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						Disorders"). Highly preferred
HMIAP86 1283 Production of MIP-1alpha FMAT. Assays MIP1alpha for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						indications include neoplasms
HMIAP86 1283 Production of for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						and cancers, such as, leukemia,
HMIAP86 1283 Production of for immunomodulatory MIP1alpha proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be		· ·				lymphoma, prostate, breast,
HMIAP86 1283 Production of MIP-lalpha FMAT. Assays MIP1alpha for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						lung, colon, pancreatic,
HMIAP86 1283 Production of for immunomodulatory MIP1alpha proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						esophageal, stomach, brain,
HMIAP86 1283 Production of for immunomodulatory MIP1alpha proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						liver, and urinary cancer. Other
HMIAP86 1283 Production of for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						preferred indications include
HMIAP86 1283 Production of for immunomodulatory MIP1alpha proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						benign dysproliferative
HMIAP86 1283 Production of MIP-1alpha FMAT. Assays MIP1alpha for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						disorders and pre-neoplastic
HMIAP86 1283 Production of MIP-1alpha FMAT. Assays MIP1alpha for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						conditions, such as, for
HMIAP86 1283 Production of MIP-1alpha FMAT. Assays MIP1alpha for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						example, hyperplasia,
HMIAP86 1283 Production of MIP-1alpha FMAT. Assays MIP1alpha for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be						metaplasia, and/or dysplasia.
MIP1alpha for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be		HMIAP86	1283	Production of	MIP-1alpha FMAT. Assays	A highly preferred
proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be	335			MIP1alpha	for immunomodulatory	embodiment of the invention
				1	proteins produced by activated	includes a method for
					dendritic cells that upregulate	stimulating MIP1a production.
					monocyte/macrophage and T	An alternative highly preferred
					cell chemotaxis are well	embodiment of the invention
					known in the art and may be	includes a method for

inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is	infection (e.g., an infectious disease as described below	under "Infectious Disease"). Preferred indications include	blood disorders (e.g., as described below under		Related Disorders", and/or "Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous
used or routinely modified to assess the ability of polypeptides of the invention	(including antibodies and agonists or antagonists of the	invention) to mediate immunomodulation, modulate	cell differentiation. Exemplary	assays that test for	immunomodulatory proteins evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and
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		45/1).0 10 /2001). Dustran	discoso consis nontroponio
		43(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
		29 (2000); Verhasselt et al., J	suppression of immune
		Immunol 158:2919-2925	reactions to transplanted
		(1997); and Nardelli et al., J	organs and tissues, hemophilia,
		Leukoc Biol 65:822-828	hypercoagulation, diabetes
		(1999), the contents of each of	mellitus, endocarditis,
		which are herein incorporated	meningitis, Lyme Disease,
		by reference in its entirety.	asthma, and allergy.
		Human dendritic cells that may	Preferred indications also
		be used according to these	include neoplastic diseases
		assays may be isolated using	(e.g., leukemia, lymphoma,
		techniques disclosed herein or	and/or as described below
		otherwise known in the art.	under "Hyperproliferative
		Human dendritic cells are	Disorders"). Highly preferred
		antigen presenting cells in	indications include neoplasms
		suspension culture, which,	and cancers, such as, leukemia,
		when activated by antigen	lymphoma, prostate, breast,
		and/or cytokines, initiate and	lung, colon, pancreatic,
	•	upregulate T cell proliferation	esophageal, stomach, brain,
		and functional activities.	liver, and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
HMIAP86   1283   Pro	3 Production of TNF	TNFa FMAT. Assays for	A highly preferred
335   alph	alpha by dendritic	immunomodulatory proteins	embodiment of the invention
cell	cells	produced by activated	includes a method for

																							_							
inhibiting (e.g., decreasing)	TNF alpha production. An	alternative highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly
macrophages, T cells,	fibroblasts, smooth muscle,	and other cell types that exert a	wide variety of inflammatory	and cytotoxic effects on a	variety of cells are well known	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J
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Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),
	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel

disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Highly preferred indications include eosinophilia, asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders.  In in the art indications include immune and hematopoietic disorders (e.g., as described below under the ability "Immune Activity", and "Blood-Related Disorders"), agantibodies autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s ls are a type disease, multiple sclerosis and/or as described below), they are
,	Assay that measures the production of the chemokine interleukin-8 (IL-8) from immune cells (such as the EOL-1 human eosinophil cell line) are well known in the art (for example, measurement of IL-8 production by FMAT) and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit. Eosinophils are a type of immune cell important in alleroic responses: they are
	Production of IL-8 by immune cells (such as the human EOL-1 eosinophil cells)
	1283
	HMIAP86
	335

				recruited to tissues and mediate the inflammtory	described below). Highly preferred indications also
				response of late stage allergic reaction. IL8 is a strong	include boosting or inhibiting immune cell proliferation.
_				immunomodulator and may	Preferred indications include
				have a potential	neoplastic diseases (e.g.,
-				prointlanmatory role in	leukemia, iyinphonia, anu/or as described helow under
				disorders (such as allergy and	"Hyperproliferative
				asthma).	Disorders"). Highly preferred
				`	indications include boosting an
					eosinophil-mediated immune
					response, and suppressing an
					eosinophil-mediated immune
					response.
HMIAP86	98	1283	IL-10 in Human T-cell 2B9		
HMIAP86	98,	1283	Production of IL-8	Assays measuring production	Highly preferred indications
			by by endothelial	of IL-8 are well known in the	include immunological and
			cells (such as	art and may be used or	inflammatory disorders (e.g.,
			Human Umbilical	routinely modified to assess	such as allergy, asthma,
			Cord Endothelial	the ability of polypeptides of	leukemia, etc. and as described
<u>.                                    </u>			Cells).	the invention (including	below under "Immune
- 41		1.00		antibodies and agonists or	Activity", and "Blood-Related
				antagonists of the invention) to	Disorders"). Highly preferred
				regulate production and/or	indications also includie
		_		secretion of IL-8. For	autoimmune disorders (e.g.,
				example, FMAT may be used	rheumatoid arthritis, systemic
_				or routinely modified to assess	lupus erythematosis, Crohn"s
				the ability of polypeptides of	disease, multiple sclerosis
		-1		the invention (including	and/or as described below),

				antibodies and agonists or	neoplastic disorders (e.g.,
			244	antagonists of the invention) to	organ cancers such as lung,
·				regulate production and/or	liver, colon cancer, and/or as
				secretion of IL-8 from	described below under
				endothelial cells (such as	"Hyperproliferative
				human umbilical vein	Disorders"), and
				endothelial cells (HUVEC)).	cardiovascular disorders (e.g.
				HUVECs are endothelial cells	such as described below under
				which line venous blood	"Cardiovascular Disorders").
				vessels, and are involved in	Preferred indications include
				functions that include, but are	thrombosis, bacteremia and
				not limited to, angiogenesis,	sepsis syndrome and
				vascular permeability, vascular	consequent complications
	_			tone, and immune cell	(such as acute respiratory
				extravasation. Endothelial	distress syndrome and
				cells play a pivotal role in the	systemic ischemia-reperfusion
	-			initiation and perpetuation of	resulting from septic shock),
				inflammation and secretion of	restnosis and atherosclerosis.
				IL-8 may play an important	
				role in recruitment and	
				activation of immune cells	
				such as neutrophils,	
				macrophages, and	
	HMIAP86	1283	Production of	Assays for measuring	Highly preferred indications
335			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and

inflammatory disorders, immunological disorders,	neoplastic disorders (e.g.	cancer/tumorigenesis), and	cardiovascular disorders (such	as described below under	"Immune Activity", "Blood-	Related Disorders",	"Hyperproliferative Disorders"	and/or "Cardiovascular	Disorders"). Highly preferred	indications include neoplasms	and cancers such as, for	example, leukemia, lymphoma,	melanoma, renal cell	carcinoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.						
agonists or antagonists of the invention) to regulate VCAM	expression. For example,	FMAT may be used to meaure	the upregulation of cell surface	VCAM-1 expresssion in	endothelial cells. Endothelial	cells are cells that line blood	vessels, and are involved in	functions that include, but are	not limited to, angiogenesis,	vascular permeability, vascular	tone, and immune cell	extravasation. Exemplary	endothelial cells that may be	used according to these assays	include human umbilical vein	endothelial cells (HUVEC),	which are available from	commercial sources. The	expression of VCAM	(CD106), a membrane-	associated protein, can be	upregulated by cytokines or	other factors, and contributes	to the extravasation of	lymphocytes, leucocytes and	other immune cells from blood	vessels; thus VCAM	expression plays a role in	nromoting immine and
								,														-							
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				inflammatory responses.	
	HMKCG09	1284	Regulation of	Assays for the regulation (i.e.	Highly preferred indications
336			viability or	increases or decreases) of	include eosinophilia, asthma,
			proliferation of	viability and proliferation of	allergy, hypersensitivity
			immune cells (such	cells in vitro are well-known in	reactions, inflammation, and
			as human	the art and may be used or	inflammatory disorders.
			eosinophil EOL-1	routinely modified to assess	Additional highly preferred
			cells).	the ability of polypeptides of	indications include immune
				the invention (including	and hematopoietic disorders
				antibodies and agonists or	(e.g., as described below under
				antagonists of the invention) to	"Immune Activity", and
				regulate viability and	"Blood-Related Disorders"),
				proliferation of eosinophil cells	autoimmune diseases (e.g.,
				and cell lines. For example,	rheumatoid arthritis, systemic
				the CellTiter-Gloô	lupus erythematosis, Crohn"s
				Luminescent Cell Viability	disease, multiple sclerosis
				Assay (Promega Corp.,	and/or as described below),
				Madison, WI, USA) can be	immunodeficiencies (e.g., as
				used to measure the number of	described below). Highly
	A-92			viable cells in culture based on	preferred indications also
				quantitation of the ATP	include boosting or inhibiting
				present which signals the	immune cell proliferation.
				presence of metabolically	Preferred indications include
				active cells. Eosinophils are a	neoplastic diseases (e.g.,
				type of immune cell important	leukemia, lymphoma, and/or as
				in allergic responses; they are	described below under
				recruited to tissues and	"Hyperproliferative
				mediate the inflammtory	Disorders"). Highly preferred
				response of late stage allergic	indications include boosting an
				reaction. Eosinophil cell lines	eosinophil-mediated immune
				that may be used according to	response, and suppressing an

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eosinophil-mediated immune response.	A highly preferred embodiment of the invention	includes a method for	IFNg. An alternative highly	preferred embodiment of the	invention includes a method	Ior inhibiting the production of IFNg. Highly preferred	S	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or as	described below under	"Infectious Disease"). Highly	preferred indications include
these assays are publicly available and/or may be routinely generated.  Exemplary eosinophil cells that may be used according to these assays include EOL-1 Cells.	IFNgamma FMAT. IFNg plays a central role in the immune	system and is considered to be	IFNg promotes TH1 and	inhibits TH2 differentiation;	promotes IgG2a and inhibits	ige secretion; induces macrophage activation; and	increases MHC expression.	Assays for immunomodulatory	proteins produced by T cells	and NK cells that regulate a	variety of inflammatory	activities and inhibit TH2	helper cell functions are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	imminomodulation regulate
	Production of IFNgamma using a	T cells																			
	1284	•																			
	HMKCG09																				
	336																		-		

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			inflammatory activities,	autoimmune disease (e.g.,
			modulate TH2 helper cell	rheumatoid arthritis, systemic
			function, and/or mediate	lupus erythematosis, multiple
			humoral or cell-mediated	sclerosis and/or as described
			immunity. Exemplary assays	below), immunodeficiency
			that test for	(e.g., as described below),
-			immunomodulatory proteins	boosting a T cell-mediated
			evaluate the production of	immune response, and
			cytokines, such as Interferon	suppressing a T cell-mediated
			gamma (IFNg), and the	immune response. Additional
			activation of T cells. Such	highly preferred indications
			assays that may be used or	include inflammation and
			routinely modified to test	inflammatory disorders.
			immunomodulatory activity of	Additional preferred
			polypeptides of the invention	indications include idiopathic
			(including antibodies and	pulmonary fibrosis. Highly
			agonists or antagonists of the	preferred indications include
			invention) include the assays	neoplastic diseases (e.g.,
			disclosed in Miraglia et al., J	leukemia, lymphoma,
			Biomolecular Screening 4:193-	melanoma, and/or as described
			204 (1999); Rowland et al.,	below under
			"Lymphocytes: a practical	"Hyperproliferative
			approach" Chapter 6:138-160	Disorders"). Highly preferred
		_	(2000); Gonzalez et al., J Clin	indications include neoplasms
			Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
			Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
	3.7		Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
-			et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
			15:749-795 (1997), and	esophageal, stomach, brain,
			Rheumatology (Oxford)	liver and urinary cancer. Other
			38(3):214-20 (1999), the	preferred indications include

				contents of each of which are	benign dysproliferative
				herein incorporated by	disorders and pre-neoplastic
	-			reference in its entirety.	conditions, such as, for
				Human T cells that may be	example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
			-	techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
				human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
		-		CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
		•••		be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
			-		organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HMKCG09	1284	Production of IL-10	Assays for production of IL-10	Highly preferred indications
336			and activation of T-	and activation of T-cells are	include allergy and asthma.
, ,			cells.	well known in the art and may	Additional highly preferred
				be used or routinely modified	indications include immune
				to assess the ability of	and hematopoietic disorders
_				polypeptides of the invention	(e.g., as described below under
				(including antibodies and	"Immune Activity", and
				agonists or antagonists of the	"Blood-Related Disorders"),
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	invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for example, assays such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "T-helper type 2 cell-directed therapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response.
	secreted from 1h2 cells may be measured as a marker of Th2 cell activation Th2 cells are	

		A nignty preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a method for
a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.		Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be
	TNFa in Human T-cell 293T	Activation of Natural Killer Cell ERK Signaling Pathway.
	1285	1285
	HMMAH60	НММАН60
	337	337

	used or routinely modified to	inhihiting natural killer cell
 	about the following the state of the state o	1:00 11:-1:-:
 	test EKK kinase-induced	differentiation. Highly
	activity of polypeptides of the	preferred indications include
	invention (including antibodies	neoplastic diseases (e.g., as
 	and agonists or antagonists of	described below under
 	the invention) include the	"Hyperproliferative
 	assays disclosed in Forrer et	Disorders"), blood disorders
 ,	al., Biol Chem 379(8-9):1101-	(e.g., as described below under
	1110 (1998); Kyriakis JM,	"Immune Activity",
 	Biochem Soc Symp 64:29-48	"Cardiovascular Disorders",
	(1999); Chang and Karin,	and/or "Blood-Related
	Nature 410(6824):37-40	Disorders"), immune disorders
-	(2001); and Cobb MH, Prog	(e.g., as described below under
 -	Biophys Mol Biol 71(3-4):479-	"Immune Activity") and
-	500 (1999); the contents of	infections (e.g., as described
-	each of which are herein	below under "Infectious
-	incorporated by reference in its	Disease"). Preferred
-	entirety. Natural killer cells	indications include blood
 	that may be used according to	disorders (e.g., as described
_	these assays are publicly	below under "Immune
 -	available (e.g., through the	Activity", "Blood-Related
	ATCC). Exemplary natural	Disorders", and/or
	killer cells that may be used	"Cardiovascular Disorders").
 	according to these assays	Highly preferred indications
	include the human natural	include autoimmune diseases
 	killer cell lines (for example,	(e.g., rheumatoid arthritis,
	NK-YT cells which have	systemic lupus erythematosis,
 	eytolytic and cytotoxic	multiple sclerosis and/or as
-	activity) or primary NK cells.	described below) and
 		immunodeficiencies (e.g., as
		described below). Additional

				highly preferred indications	indications
				include inflammation and	ation and
				inflammatory disorders.	sorders.
				Highly preferred indications	d indications
				also include cancers such as,	cers such as,
				kidney, melanoma, prostate,	ma, prostate,
				breast, lung, colon, pancreatic,	on, pancreatic,
				esophageal, stomach, brain,	nach, brain,
				liver, urinary cancer,	ncer,
				Iymphoma and leukemias.	leukemias.
				Other preferred indications	indications
				include benign	include benign dysproliferative
				disorders and pre-neoplastic	re-neoplastic
				conditions, such as, for	as, for
				example, hyperplasia,	plasia,
				metaplasia, and/or dysplasia.	or dysplasia.
				Other highly preferred	eferred
				indications include,	nde,
				pancytopenia, leukopenia,	eukopenia,
				leukemias, Hodgkin's disease,	gkin's disease,
				acute lymphocytic anemia	tic anemia
				(ALL), arthritis, asthma,	, asthma,
				AIDS, granulomatous disease,	natous disease,
				inflammatory bowel disease,	owel disease,
				sepsis, psoriasis, immune	, immune
				reactions to transplanted	splanted
				organs and tissues,	les,
				endocarditis, m	endocarditis, meningitis, Lyme
				Disease, and allergies.	ergies.
337	HMMAH60	1285	VEGF in SW480		

	HMMAH60	1285	Production of IL-10	Assays for production of IL-10	Highly preferred indications
337			and activation of T-	and activation of T-cells are	include allergy and asthma.
			cells.	well known in the art and may	Additional highly preferred
				be used or routinely modified	indications include immune
				to assess the ability of	and hematopoietic disorders
				polypeptides of the invention	(e.g., as described below under
			-	(including antibodies and	"Immune Activity", and
				agonists or antagonists of the	"Blood-Related Disorders"),
				invention) to stimulate or	autoimmune diseases (e.g.,
				inhibit production of IL-10	rheumatoid arthritis, systemic
				and/or activation of T-cells.	lupus erythematosis, Crohn"s
				Exemplary assays that may be	disease, multiple sclerosis
				used or routinely modified to	and/or as described below),
				assess the ability of	immunodeficiencies (e.g., as
				polypeptides and antibodies of	described below), boosting a T
				the invention (including	cell-mediated immune
				agonists or antagonists of the	response, and suppressing a T
				invention) to modulate IL-10	cell-mediated immune
			,	production and/or T-cell	response.
				proliferation include, for	
				example, assays such as	
				disclosed and/or cited in:	
				Robinson, DS, et al., "Th-2	
				cytokines in allergic disease"	
				Br Med Bull; 56 (4): 956-968	
			,,	(2000), and Cohn, et al., "T-	
				helper type 2 cell-directed	
				therapy for asthma"	
				Pharmacology & Therapeutics;	
				88: 187-196 (2000); the	
!				contents of each of which are	

	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is
herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL 10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL 10, IL 13, IL 5 and IL 6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	Production of MIP1alpha
	1286
	НМQDF12
	338

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infection (e.g., an infectious	disease as described below	under "Infectious Disease").	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	
(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, modulate	chemotaxis, and modulate T	cell differentiation. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et	
				•																		_								
																										- 14				_

HMQDF12

	wide variety of inflammatory	embodiment of the invention	$\overline{}$
	and extotoxic effects on a	includes a method for	
	und ej totoate effects off a	etimulating (a.g. increasing)	
	vallety of cells are well kilowil	stillulating (e.g., ilicicasing)	
	in the art and may be used or	TNF alpha production.	
	routinely modified to assess	Highly preferred indications	
	the ability of polypeptides of	include blood disorders (e.g.,	
	the invention (including	as described below under	
	antibodies and agonists or	"Immune Activity", "Blood-	
	antagonists of the invention) to	Related Disorders", and/or	
	mediate immunomodulation,	"Cardiovascular Disorders"),	
	modulate inflammation and	Highly preferred indications	
	cytotoxicity. Exemplary	include autoimmune diseases	
	assays that test for	(e.g., rheumatoid arthritis,	
	immunomodulatory proteins	systemic lupus erythematosis,	
	evaluate the production of	Crohn"s disease, multiple	
	cytokines such as tumor	sclerosis and/or as described	
	necrosis factor alpha (TNFa),	below), immunodeficiencies	
	and the induction or inhibition	(e.g., as described below),	
	of an inflammatory or	boosting a T cell-mediated	
	cytotoxic response. Such	immune response, and	
	assays that may be used or	suppressing a T cell-mediated	
	routinely modified to test	immune response. Additional	
	immunomodulatory activity of	highly preferred indications	
	polypeptides of the invention	include inflammation and	
	(including antibodies and	inflammatory disorders, and	
	agonists or antagonists of the	treating joint damage in	
	invention) include assays	patients with rheumatoid	
	disclosed in Miraglia et al., J	arthritis. An additional highly	
 	Biomolecular Screening 4:193-	preferred indication is sepsis.	
	204(1999); Rowland et al.,	Highly preferred indications	
	"Lymphocytes: a practical	include neoplastic diseases	_

reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	
	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its
	Inhibition of squalene synthetase gene transcription.
	1286
	HMQDF12
	338

- videt				entirety.	
338	НМQDF12	1286	Caspase (+paclitaxel) in SW480		
339	HMSBX80	1287	CD71 in Human T cells		
	HMSFS21	1288	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
340				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
	-			assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
	74.00			(including antibodies and	lupus erythematosis, multiple

		Secondary on automate of M	1 1
	,	agomists of amagomists of the	scierosis and/or as described
		invention) to mediate	below) and
		immunomodulation and	immunodeficiencies (e.g., as
		differentiation and modulate T	described below). Highly
	-	cell proliferation and function.	preferred indications also
		Exemplary assays that test for	include boosting a B cell-
		immunomodulatory proteins	mediated immune response
		evaluate the production of	and alternatively suppressing a
		cytokines, such as IL-6, and	B cell-mediated immune
		the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
		proliferation and functional	inflammation and
		activities. Such assays that	inflammatory
		may be used or routinely	disorders. Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include
		polypeptides of the invention	neoplastic diseases (e.g.,
		(including antibodies and	myeloma, plasmacytoma,
-		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
		"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
		Immunol 158:2919-2925	lymphoma, melanoma, and
		(1997), the contents of each of	prostate, breast, lung, colon,
		which are herein incorporated	pancreatic, esophageal,
		by reference in its entirety.	stomach, brain, liver and

				Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred infectious disease as described below under "Infectious
340	HMSFS21	1288	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may	Preferred embodiments of the invention include using polypeptides of the invention

				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
				expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
				(2001); and, Miyamoto K, et	
	-			al., Am J Pathol, 156(5):1733-	
				1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
· pe				used according to these assays	
				are publicly available (e.g.,	
				through the ATCC) and/or	
				may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include microvascular	
				endothelial cells (MVEC).	
	HMSGB14	1289	Activation of	Assays for the activation of	Preferred indications
341			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are known in	(e.g., as described below under
			response element in	the art and may be used or	"Hyperproliferative
			immune cells (such	routinely modified to assess	Disorders"), blood disorders
				•	

as T-cells).	the ability of polypeptides of	(e.g., as described below under
	the invention (including	"Immune Activity",
	antibodies and agonists or	"Cardiovascular Disorders",
	antagonists of the invention) to	and/or "Blood-Related
	modulate growth and other cell	Disorders"), and infection
	functions. Exemplary assays	(e.g., an infectious disease as
	for transcription through the	described below under
	AP1 response element that	"Infectious Disease"). Highly
	may be used or routinely	preferred indications include
	modified to test AP1-response	autoimmune diseases (e.g.,
	element activity of	rheumatoid arthritis, systemic
	polypeptides of the invention	lupus erythematosis, multiple
	(including antibodies and	sclerosis and/or as described
	agonists or antagonists of the	below) and
	invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety. T	lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,

				according to these assays are publicly available (e.g.,	liver, and urinary cancer. Other preferred indications include
				through the ATCC).	benign dysproliferative
				Exemplary mouse T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the CTLL cell	example, hyperplasia,
				line, which is an IL-2	metaplasia, and/or dysplasia.
				dependent suspension-culture	Preferred indications include
				cell line with cytotoxic	arthritis, asthma, AIDS,
				activity.	allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
			-		myeloma, Burkitt's lymphoma,
					granulomatous disease,
-					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HMSGT42	1290	Activation of	Kinase assay. JNK and p38	A highly preferred
342			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
				the art and may be used or	preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred

	antibodies and agonists or	embodiment of the invention
	antagonists of the invention) to	includes a method for
	promote or inhibit cell	stimulating endothelial cell
	proliferation, activation, and	proliferation. An alternative
	apoptosis. Exemplary assays	highly preferred embodiment
	for JNK and p38 kinase	of the invention includes a
	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
	assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
-	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	Exemplary endothelial cells	embodiment of the invention

includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for	inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for reducing cardiac hypertrophy. An alternative	highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly	preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of	the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular	dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic
that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line	venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone.	and immune cell extravasation.			

			hemodynamic overload and/or
		-	as described below under
			"Condigues Delow under
			Cardiovascular Disorders ).
			Highly preferred indications
			include cardiovascular,
			endothelial and/or angiogenic
			disorders (e.g., systemic
			disorders that affect vessels
			such as diabetes mellitus, as
			well as diseases of the vessels
			themselves, such as of the
			arteries, capillaries, veins
			and/or lymphatics). Highly
			preferred are indications that
			stimulate angiogenesis and/or
			cardiovascularization. Highly
-			preferred are indications that
			inhibit angiogenesis and/or
			cardiovascularization.
			Highly preferred indications
			include antiangiogenic activity
			to treat solid tumors,
			leukemias, and Kaposi"s
			sarcoma, and retinal disorders.
			Highly preferred indications
			include neoplasms and cancer,
			such as, Kaposi"s sarcoma,
			hemangioma (capillary and
	-		cavernous), glomus tumors,
			telangiectasia, bacillary
			angiomatosis,

hemangioendothelioma, angiosarcoma,	haemangiopericytoma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease.
										-			-											44.			

and cancer. Highly preferred indications also	include trauma such as	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include
																				**			-					
																												;

blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	blood disorders (e.g., as described below under may "Immune Activity", "Blood-fied Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disorders").
	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase the activation of the invention of t
	Activation of transcription through cAMP response element in immune cells (such as T-cells).
	1291
	HMSHM14
	343

			and regulate CREB	indications include
			transcription factors, and	autoimmune diseases (e.g.,
			modulate expression of genes	rheumatoid arthritis, systemic
			involved in a wide variety of	lupus erythematosis, multiple
	_		cell functions. Exemplary	sclerosis and/or as described
			assays for transcription	below), immunodeficiencies
			through the cAMP response	(e.g., as described below),
			element that may be used or	boosting a T cell-mediated
		.,,,,	routinely modified to test	immune response, and
			cAMP-response element	suppressing a T cell-mediated
			activity of polypeptides of the	immune response. Additional
			invention (including antibodies	preferred indications include
			and agonists or antagonists of	inflammation and
			the invention) include assays	inflammatory disorders.
			disclosed in Berger et al., Gene	Highly preferred indications
			66:1-10 (1998); Cullen and	include neoplastic diseases
			Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
		-	216:362-368 (1992); Henthorn	and/or as described below
			et al., Proc Natl Acad Sci USA	under "Hyperproliferative
			85:6342-6346 (1988); Black et	Disorders"). Highly preferred
			al., Virus Genes 15(2):105-117	indications include neoplasms
	·		(1997); and Belkowski et al., J	and cancers, such as, for
			Immunol 161(2):659-665	example, leukemia, lymphoma
			(1998), the contents of each of	(e.g., T cell lymphoma,
			which are herein incorporated	Burkitt's lymphoma, non-
			by reference in its entirety. T	Hodgkins lymphoma,
_			cells that may be used	Hodgkin"s disease),
	-		according to these assays are	melanoma, and prostate,
			publicly available (e.g.,	breast, lung, colon, pancreatic,
			through the ATCC).	esophageal, stomach, brain,
			Exemplary mouse T cells that	liver and urinary cancer. Other

				may be used according to these	preferred indications include
				assays include the CTLL cell	benign dysproliferative
				line, which is a suspension	disorders and pre-neoplastic
				culture of IL-2 dependent	conditions, such as, for
				cytotoxic T cells.	example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
-					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HMSHM14	1291	Activation of	Assays for the activation of	A preferred embodiment of
343			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,

	antibodi	antibodies and agonists or	increasing) TNF alpha
	antagoni	n) to	production. Preferred
	regulate	regulate the serum response	indications include blood
	factors a	factors and modulate the	disorders (e.g., as described
	expression	expression of genes involved	below under "Immune
	in growt	in growth. Exemplary assays	Activity", "Blood-Related
	for trans	for transcription through the	Disorders", and/or
	SRE that	SRE that may be used or	"Cardiovascular Disorders"),
	routinely	routinely modified to test SRE	Highly preferred indications
	activity	activity of the polypeptides of	include autoimmune diseases
	the inver	the invention (including	(e.g., rheumatoid arthritis,
	antibodie	antibodies and agonists or	systemic lupus erythematosis,
	antagoni	antagonists of the invention)	Crohn"s disease, multiple
	include a	include assays disclosed in	sclerosis and/or as described
	Berger e	Berger et al., Gene 66:1-10	below), immunodeficiencies
-	(1998);	(1998); Cullen and Malm,	(e.g., as described below),
	Methods	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (199	368 (1992); Henthorn et al.,	immune response, and
	Proc Nat	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342	85:6342-6346 (1988); and	immune response. Additional
	Black et	Black et al., Virus Genes	highly preferred indications
	12(2):10	12(2):105-117 (1997), the	include inflammation and
	content	content of each of which are	inflammatory disorders, and
	herein in	herein incorporated by	treating joint damage in
	reference	reference in its entirety. T	patients with rheumatoid
	cells that	cells that may be used	arthritis. An additional highly
	accordin	according to these assays are	preferred indication is sepsis.
	publicly	publicly available (e.g.,	Highly preferred indications
	through	through the ATCC).	include neoplastic diseases
	Exempla	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be u	may be used according to these	and/or as described below

		assays include the CTLL cell	under "Hyperproliferative
-		line, which is an IL-2	Disorders"). Additionally,
		 dependent suspension culture	highly preferred indications
		 of T cells with cytotoxic	include neoplasms and
-		 activity.	cancers, such as, for example,
			leukemia, lymphoma,
			melanoma, glioma (e.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
	-		liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
		 	conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
,-			Preferred indications include
			anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
- Lab			lymphocytic anemia (ALL),
_			plasmacytomas, multiple
		 	myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
		 	disease, inflammatory bowel
			disease, neutropenia,
-			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted

organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing)  MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing)  MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred infiammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as
	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation.  Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as
	Production of MCP-1
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	HMSHM14
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	protein	protein (MCP), and the	"Immune Activity". "Blood-
	activation	activation of monocytes and T	Related Disorders", and/or
	cells. Su	cells. Such assays that may be	"Cardiovascular Disorders").
	used or re	used or routinely modified to	Highly preferred indications
	test imm	test immunomodulatory and	include autoimmune diseases
	diffferent	diffferentiation activity of	(e.g., rheumatoid arthritis,
	polypepti	polypeptides of the invention	systemic lupus erythematosis,
	(includin	(including antibodies and	multiple sclerosis and/or as
-	agonists	agonists or antagonists of the	described below) and
	invention	invention) include assays	immunodeficiencies (e.g., as
	disclosed	disclosed in Miraglia et al., J	described below). Preferred
	Biomolec	Biomolecular Screening 4:193-	indications also include
	204(1999	204(1999); Rowland et al.,	anemia, pancytopenia,
	"Lymphc	"Lymphocytes: a practical	leukopenia, thrombocytopenia,
	approach	approach" Chapter 6:138-160	Hodgkin's disease, acute
	(2000); 8	(2000); Satthaporn and	lymphocytic anemia (ALL),
	Eremin,	Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
-	45(1):9-1	45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
	Verhasse	Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
	158:2919	158:2919-2925 (1997), the	disease, inflammatory bowel
	contents	contents of each of which are	disease, sepsis, neutropenia,
	herein in	herein incorporated by	neutrophilia, psoriasis,
	reference	reference in its entirety.	suppression of immune
	Human d	Human dendritic cells that may	reactions to transplanted
	be used a	be used according to these	organs and tissues,
	assays m	assays may be isolated using	hemophilia, hypercoagulation,
	technique	techniques disclosed herein or	diabetes mellitus, endocarditis,
	otherwise	otherwise known in the art.	meningitis (bacterial and
	Human d	Human dendritic cells are	viral), Lyme Disease, asthma,
	antigen p	antigen presenting cells in	and allergy Preferred
	suspensic	suspension culture, which,	indications also include

				when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
344	HMSHS36	1292	Activation of JNK Signaling Pathway in immune cells (such as eosinophils).	Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis.  Exemplary assays for JNK	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s

		kinase activity that may be	disease, multiple sclerosis
		 used or routinely modified to	and/or as described below),
		 test JNK kinase-induced	immunodeficiencies (e.g., as
		 activity of polypeptides of the	described below). Highly
		 invention (including antibodies	preferred indications also
	_	 and agonists or antagonists of	include boosting or inhibiting
		the invention) include the	immune cell proliferation.
		assays disclosed in Forrer et	Preferred indications include
		al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
		1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
		Cell Res 247(2): 495-504	described below under
		(1999); Kyriakis JM, Biochem	"Hyperproliferative
		Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
		 Chang and Karin, Nature	indications include boosting an
		410(6824):37-40 (2001); and	eosinophil-mediated immune
		Cobb MH, Prog Biophys Mol	response, and suppressing an
		   Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
		 the contents of each of which	response.
		are herein incorporated by	
		 reference in its entirety.	
		 Exemplary cells that may be	
		used according to these assays	
		 include eosinophils.	
		Eosinophils are important in	
-		the late stage of allergic	
		reactions; they are recruited to	
		tissues and mediate the	
		inflammatory response of late	
		 stage allergic reaction.	
		 Moreover, exemplary assays	
	3	that may be used or routinely	

modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt 1):565-74; and,	Sousa AR, et al., "In vivo	resistance to corticosteroids in	bronchial asthma is associated	with enhanced	phosyphorylation of JUN N-	terminal kinase and failure of
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															20															

				prednisolone to inhibit JUN N-	
				terminal kinase	
				phosphorylation" J Allergy	
				Clin Immunol; Sep;104(3 Pt	
			-	1):565-74 (1999); the contents	
				of each of which are herein	
				incorporated by reference in its	
				entirety.	
	HMSHS36	1292	Activation of	Assays for the activation of	Highly preferred indications
344			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
			response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
			cells).	modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
			-	immunomodulatory functions.	cell-mediated immune
		·		Exemplary assays for	response, and suppressing a T
		-		transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an

		"Hyperproliferative Disorders"), Preferred	indications include neoplasms and cancers, such as, for	example, leukemia, lymphoma, and prostate, breast, lung,	colon, pancreatic, esophageal,	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),		myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,
agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med	182(3):801-810 (1995); De Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. NK	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to	these assays include the NK-	YT cell line, which is a human	natural killer cell line with	cytolytic and cytotoxic	activity.	
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								-									-			

neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below) immunodeficiencies
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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	HMSHS36
	344

					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
-					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
344	HMSHS36	1292	SEAP in NK16/STAT6		
	HMSJM65	1293	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
345				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for

IgE production and increases IL-6 production. An alternative IgA production (IgA plays a highly preferred embodiment of the invention includes a	ells. IL-6	 ory	ه	expression level is strongly "Cardiovascular Disorders"), regulated by cytokines, growth and infection (e.g., as	factors, and hormones are well described below under known in the art and may be "Infectious Disease"). Highly	used or routinely modified to preferred indications include assess the ability of autoimmune diseases (e.g.,	polypeptides of the invention   rheumatoid arthritis, systemic   (including antibodies and   lupus erythematosis, multiple	the	nd odulate T	cell proliferation and function. preferred indications also Exemplary assays that test for include boosting a B cell-	St	evaluate the production of and alternatively suppressing
					-							

the stimulation and	response.	response. Highly preferred
upregulation of T cell	indication	indications include
proliferation and functional		tion and
activities. Such assays that		ıtory
may be used or routinely		disorders.Additional highly
modified to test	preferred	preferred indications include
immunomodulatory and		asthma and allergy. Highly
diffferentiation activity of		preferred indications include
polypeptides of the invention		neoplastic diseases (e.g.,
(including antibodies and		myeloma, plasmacytoma,
agonists or antagonists of the		leukemia, lymphoma,
invention) include assays		melanoma, and/or as described
disclosed in Miraglia et al., J	et al., J   below under	der
Biomolecular Screening 4:193-		"Hyperproliferative
204(1999); Rowland et al.,		Disorders"). Highly preferred
"Lymphocytes: a practical		indications include neoplasms
approach" Chapter 6:138-160		and cancers, such as, myeloma,
(2000); and Verhasselt et al., J		plasmacytoma, leukemia,
Immunol 158:2919-2925		lymphoma, melanoma, and
(1997), the contents of each of		prostate, breast, lung, colon,
which are herein incorporated	per	pancreatic, esophageal,
by reference in its entirety.		stomach, brain, liver and
Human dendritic cells that may		urinary cancer. Other preferred
be used according to these		indications include benign
assays may be isolated using		dysproliferative disorders and
techniques disclosed herein or	_	pre-neoplastic conditions, such
otherwise known in the art.		as, for example, hyperplasia,
Human dendritic cells are		metaplasia, and/or dysplasia.
antigen presenting cells in	-	Preferred indications include
suspension culture, which,		anemia, pancytopenia,
when activated by antigen		leukopenia, thrombocytopenia,

-	the Highly preferred indications include asthma, allergy, hypersensitivity reactions, and inflammation. Preferred indications include infection (e.g., an infectious disease as invention es and "Infectious Disease"), inflammation and inflammation and inflammatory disorders (e.g., a described below under as and inflammatory disorders (e.g., an of
and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Activation of transcription through the through NFKB response element in mell-known in the art and may immune cells (such as EOL1 cells).  Polypeptides of the invention (including antibodies and agonists or antagonists of the invention modulate expression of transcription factors and modulate expression of
	HMSJU68 1294 Act tran through the transition in
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pu	ders").	include	(e.g.,	systemic	multiple	scribed		e.g., as					-																	
"Immune Activity", and	"Blood-Related Disorders")	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below).																					
umI,,	"Bloc	Prefe	autoi	rheur	lupus	sclere	belov	immı	descr																					
immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	For example, a reporter assay	(which measures increases in	transcription inducible from a	NFkB responsive element in	EOL-1 cells) may link the	
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	_																													
																			-	.—.		•								
							·											*						·		<u>,                                     </u>				-

773		polypeptides of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
gene and binds to the NFKB transcription factor, which is upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important in the allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Eol-1 is a human eosinophil cell line.		Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective
	Glucose Production in H4IIE	Regulation of apoptosis of immune cells (such as mast cells).
	1294	1294
	HMSJU68	HMSJU68
	346	346

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and mucosal tissues throughout	the body, and their activation	via immunoglobulin E -	antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by
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	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell proliferation. In a specific embodiment of the invention includes a method for inhibiting muscle cell proliferation. In a specific embodiment, skeletal muscle
reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of
	Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway
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cell proliferation is inhibited. A preferred embodiment of the invention includes a method for stimulating muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle	cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is inhibited. Highly preferred indications include disorders of the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as	described below under "Hyperproliferative Disorders"), endocrine disorders (e.g., as described below under "Endocrine Disorders"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), blood disorders (e.g., as described below under "Immune
A prefer the inverse method cell diffe specific muscle c stimulate highly p of the in method	cell differentiation. In a specific embodiment, ske muscle cell differentiatio inhibited. Highly prefit indications include disor the musculoskeletal systems of the preferred indications included incoplastic diseases (e.g.,	described below under "Hyperproliferative Disorders"), endocrine disorders (e.g., as described below under "Endocrine Disorders"), neural disorders (e.g., as described below und "Neural Activity and Neurological Diseases"), bloodisorders (e.g., as described below under "Immune
the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incorporated by reference in its entirety. Rat myoblast cells that may be	used according to these assays are publicly available (e.g., through the ATCC).  Exemplary rat myoblast cells that may be used according to these assays include L6 cells.  L6 is an adherent rat myoblast cell line, isolated from primary	cultures of rat thigh muscle, that fuses to form multinucleated myotubes and striated fibers after culture in differentiation media.

Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), and infection (e.g., as described below under "Infectious Disease"). A biohly preferred indication is	diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic	nephropathy, kıdney dısease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve	disease and nerve damage (e.g, due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma,
			·

heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infections	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.
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Additional highly preferred	indications are disorders of the	musculoskeletal system	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	failure, cachexia, myxomas,	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Highly	preferred indications include	neoplasms and cancer, such as,	rhabdomyoma,	rhabdosarcoma, stomach,	esophageal, prostate, and	urinary cancer. Preferred	indications also include breast,	lung, colon, pancreatic, brain,	and liver cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as,	hyperplasia, metaplasia, and/or		dyspiasia.	dyspiasia.
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346			(+camptothecin) in SW480		
347	HMSKC04	1295	SEAP in 293/ISRE		
347	HMSKC04	1295	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988);	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia,

272(49):30806-30811 (1997);	lymphoma, and/or as described
Chang et al., Mol Cell Biol	below under
18(9):4986-4993 (1998); and	"Hyperproliferative
Fraser et al., Eur J Immunol	Disorders"). Highly preferred
29(3):838-844 (1999), the	indications include neoplasms
contents of each of which are	and cancers, such as, leukemia,
herein incorporated by	lymphoma, prostate, breast,
reference in its entirety. T	lung, colon, pancreatic,
cells that may be used	esophageal, stomach, brain,
according to these assays are	liver, and urinary cancer. Other
publicly available (e.g.,	preferred indications include
through the ATCC).	benign dysproliferative
Exemplary mouse T cells that	disorders and pre-neoplastic
may be used according to these	conditions, such as, for
assays include the CTLL cell	example, hyperplasia,
line, which is an IL-2	metaplasia, and/or dysplasia.
dependent suspension-culture	Preferred indications include
cell line with cytotoxic	arthritis, asthma, AIDS,
activity.	allergy, anemia, pancytopenia,
- Alas	leukopenia, thrombocytopenia,
	Hodgkin's disease, acute
	lymphocytic anemia (ALL),
	plasmacytomas, multiple
	myeloma, Burkitt's lymphoma,
	granulomatous disease,
	inflammatory bowel disease,
	sepsis, psoriasis, suppression
	of immune reactions to
_	transplanted organs and
	tissues, endocarditis,
	meningitis, and Lyme Disease.

1295 SEAP in HIB/CRE 1295 Activation of transcription through GATA-3 response element in immune cells (such as mast cells).		y measures Highly preferred indications					_			A3 response   Preferred indications also	known in the   include blood disorders (e.g.,		d to assess   "Immune Activity", "Blood-			onists or Preferred indications include	invention) to autoimmune diseases (e.g.,					emplary   immunodeficiencies (e.g., as		A3 response   indications include neoplastic					-
1295	EAP in HIB/CRE		-		ımune cells (such   Activation of GATA-3 in mast	mast cells). cells has been linked to	cytokine and chemokine	production. Assay	activation of transcription	through the GATA3 response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and age	antagonists of the	regulate GATA3 t	factors and modulate	expression of mast cell genes	important for immune response	development. Exe	assays for transcription	through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response	activity of polypeptides of the	
			tra	 	<u>ni</u>	as							-																_

				Illinature mast cems.	
	HMSKC04	1295	Activation of	This reporter assay measures	Highly preferred indications
347			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
			-	used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic
				transcription through the	diseases (e.g., leukemia,
				NFAT response element that	lymphoma, melanoma,
				may be used or routinely	prostate, breast, lung, colon,
				modified to test NFAT-	pancreatic, esophageal,
				response element activity of	stomach, brain, liver, and

		polypeptides of the invention	urinary tract cancers and/or as
		(including antibodies and	described below under
		agonists or antagonists of the	"Hyperproliferative
		invention) include assays	Disorders"). Other preferred
		disclosed in Berger et al., Gene	indications include benign
		66:1-10 (1998); Cullen and	dysproliferative disorders and
		Malm, Methods in Enzymol	pre-neoplastic conditions, such
		216:362-368 (1992); Henthorn	as, for example, hyperplasia,
		et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	-	85:6342-6346 (1988); De Boer	Preferred indications include
		et al., Int J Biochem Cell Biol	anemia, pancytopenia,
		31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
		et al., J Immunol	leukemias, Hodgkin's disease,
		165(12):7215-7223 (2000);	acute lymphocytic anemia
,		Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
		16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
		al., J Exp Med 188:527-537	granulomatous disease,
		(1998), the contents of each of	inflammatory bowel disease,
		which are herein incorporated	sepsis, neutropenia,
		by reference in its entirety.	neutrophilia, psoriasis,
		Mast cells that may be used	suppression of immune
		according to these assays are	reactions to transplanted
		publicly available (e.g.,	organs and tissues, hemophilia,
		through the ATCC).	hypercoagulation, diabetes
		Exemplary human mast cells	mellitus, endocarditis,
		that may be used according to	meningitis, and Lyme Disease.
		these assays include the HMC-	
		1 cell line, which is an	
		immature human mast cell line	
		established from the peripheral	

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blood of a patient with mast	cell leukemia, and exhibits	many characteristics of	immature mast cells.	RANTES FMAT. Assays for	immunomodulatory proteins	that induce chemotaxis of T	cells, monocytes, and	eosinophils are well known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	induce chemotaxis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and
				Production of	RANTES in	endothelial cells	(such as human	umbilical vein	endothelial cells	(HUVEC))																				
				1295																										
				HMSKC04						-											-		_		-					
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agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.	
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																														1295
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HMSKC04 1295 Activation of transcription through NFAT response element in immune cells (such as natural killer cells).	347			promoter (antiCD3		
		HMSKC04	1295	Activation of	Assays for the activation of	Highly preferred indications
	347			transcription	transcription through the	include blood disorders (e.g.,
response element immune cells (suo as natural killer cells).				through NFAT	Nuclear Factor of Activated T	as described below under
immune cells (sua suatural killer cells).		•		response element in	cells (NFAT) response element	"Immune Activity", "Blood-
as natural killer cells).				immune cells (such	are well-known in the art and	Related Disorders", and/or
cells).				as natural killer	may be used or routinely	"Cardiovascular Disorders").
				cells).	modified to assess the ability	Highly preferred indications
					of polypeptides of the	include autoimmune diseases
					invention (including antibodies	(e.g., rheumatoid arthritis,
		_			and agonists or antagonists of	systemic lupus erythematosis,
					the invention) to regulate	multiple sclerosis and/or as
					NFAT transcription factors and	described below),
					modulate expression of genes	immunodeficiencies (e.g., as
					involved in	described below), boosting a T
					immunomodulatory functions.	cell-mediated immune
					Exemplary assays for	response, and suppressing a T
					transcription through the	cell-mediated immune
					NFAT response element that	response. Additional highly
					may be used or routinely	preferred indications include
					modified to test NFAT-	inflammation and
					response element activity of	inflammatory disorders. An
					polypeptides of the invention	additional highly preferred
					(including antibodies and	indication is infection (e.g., an
					agonists or antagonists of the	infectious disease as described
					invention) include assays	below under "Infectious
					disclosed in Berger et al., Gene	Disease"). Preferred
					66:1-10 (1998); Cullen and	indications include neoplastic
					Malm, Methods in Enzymol	diseases (e.g., leukemia,
					216:362-368 (1992); Henthorn	lymphoma, and/or as described

et al., Proc Natl Acad Sci USA   below under 85:6342-6346 (1988); "Hyperproliferative	) Med		Boer et al., Int J Biochem Cell and cancers, such as, for	Biol 31(10):1221-1236 (1999);   example, leukemia, lymphoma,	Fraser et al., Eur J Immunol and prostate, breast, lung,	29(3):838-844 (1999); and colon, pancreatic, esophageal,	Yeseen et al., J Biol Chem stomach, brain, liver and	3),	the contents of each of which indications include benign	are herein incorporated by dysproliferative disorders and	reference in its entirety. NK   pre-neoplastic conditions, such	cells that may be used as, for example, hyperplasia,	according to these assays are metaplasia, and/or dysplasia.	publicly available (e.g., Preferred indications also	through the ATCC).   include anemia, pancytopenia,	Exemplary human NK cells   leukopenia, thrombocytopenia,	that may be used according to Hodgkin's disease, acute	these assays include the NK-   lymphocytic anemia (ALL),	ш		cytolytic and cytotoxic arthritis, AIDS, granulomatous	activity. disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	
et a   85:0	Ara	182	Boe	Bio	Fras	(29(	Yes	268	the	are	refe	cell	acc	qnd	thrc	Exe	that	thes	TY	natı	cyte	acti							

					meningitis, Lyme Disease,
	1002107			3 : ; : ; : ; : ; : ; : ; : ; : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ; - : ;	asthma and allergy.
ţ	HMSKC04	1295	Activation of	Assays for the activation of	A presence embodiment of
347		465	transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
-			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
		_		antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
	<u>.</u>			regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
_				66:1-10 (1998); Cullen and	immune response, and
_	-			Malm, Methods in Enzymol	suppressing a T cell-mediated
	-			216:362-368 (1992); Henthorn	immune response. Additional
				et al., Proc Natl Acad Sci USA	highly preferred indications

include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid	arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neonlastic diseases	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,	highly preferred indications include neoplasms and cancers, such as, for example,	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia,
85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117	(1997), the content of each of which are herein incorporated by reference in its entirety. T	according to these assays are publicly available (e.g., through the ATCC).	used according to these assays include the NK-YT cell line, which is a human natural killer	cell line with cytolytic and cytotoxic activity.		

			Exemplary assays for	described below under
			transcription through the AP1	"Infectious Disease"). Highly
			response element that may be	preferred indications include
			used or routinely modified to	autoimmune diseases (e.g.,
_			test AP1-response element	rheumatoid arthritis, systemic
			activity of polypeptides of the	lupus erythematosis, multiple
	-		invention (including antibodies	sclerosis and/or as described
			and agonists or antagonists of	below) and
			the invention) include assays	immunodeficiencies (e.g., as
			disclosed in Berger et al., Gene	described below). Additional
			66:1-10 (1988); Cullen and	highly preferred indications
			Malm, Methods in Enzymol	include inflammation and
			216:362-368 (1992); Henthorn	inflammatory disorders.
			et al., Proc Natl Acad Sci USA	Highly preferred indications
			85:6342-6346 (1988);	also include neoplastic
			Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
			272(49):30806-30811 (1997);	lymphoma, and/or as described
		-	Chang et al., Mol Cell Biol	below under
			18(9):4986-4993 (1998); and	"Hyperproliferative
			Fraser et al., Eur J Immunol	Disorders"). Highly preferred
			29(3):838-844 (1999), the	indications include neoplasms
			contents of each of which are	and cancers, such as, leukemia,
			herein incorporated by	lymphoma, prostate, breast,
			reference in its entirety.	lung, colon, pancreatic,
			Human T cells that may be	esophageal, stomach, brain,
			used according to these assays	liver, and urinary cancer. Other
			are publicly available (e.g.,	preferred indications include
			through the ATCC).	benign dysproliferative
			Exemplary human T cells that	disorders and pre-neoplastic
			may be used according to these	conditions, such as, for
			assays include the SUPT cell	example, hyperplasia,

inhibiting the activation of and/or inactivating T cells. A highly preferred	embodiment of the invention includes a method for	stimulating (e.g., increasing) IL-2 production. An alternative	highly preferred embodiment	of the invention includes a method for inhibiting (e.g.,	reducing) IL-2 production.	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Highly preferred	indications include neoplastic	diseases (e.g., melanoma, renal	cell carcinoma, leukemia,	lymphoma, and/or as described
test CD28-response element activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn   et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	McGuire and Iacobelli, J	Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	3(1):552-560 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.	
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		-									-												-		_
	<del></del>		<u>.</u>												-										

highly preferred indication is AIDS. Additional highly preferred indications include	under "Infectious Disease"). A	disease, and osteoporosis, and/or as described below	associated with granulomatous	AIDS, tuberculosis, infections	includes infection (e.g.,	A highly preferred indication	metaplasia, and/or dysplasia.	example, hyperplasia,	disorders and pre-neoplastic	benign dysproliferative	preferred indications include	liver and urinary cancer. Other	esophageal, stomach, brain,	breast. lung. colon. pancreatic.	leukemia, lymphoma (e.g., T	renal cell carcinoma),	cell carcinoma (e.g., metastatic	metastatic melanoma), renal	and cancers, such as, for	indications include neoplasms	Disorders"). Highly preferred	"Hyperproliferative	below under
				• • •																			
																					-		-

					reactions to transplanted
					organs and/or tissues, uveitis,
					psoriasis, and tropical spastic
					paraparesis. Preferred
					indications include blood
					disorders (e.g., as described
					below under "Immune
					Activity", "Blood-Related
					Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications also
					include anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
,,					lymphocytic anemia (ALL),
					plasmacytomas, multiple
<del>-</del>					myeloma, Burkitt's lymphoma,
					arthritis, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HMSKC04	1295	Activation of	Assays for the activation of	Highly preferred indications
347	·· •		transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
		•••	as T-cells).	may be used or routinely	Disorders"). Highly preferred
			./	, manual (1)	

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indications include neoplasms and cancers, such as, for	example, reukenna, rympnoma (e.g., T cell lymphoma,	Burkitt's lymphoma, non-	Hodgkins lymphoma,	Hodgkin"s disease),	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.
indicatic and can	(e.g., T	Burkitt's	Hodgkir	Hodgkir	melanor	breast, l	esophag	liver and	preferre	benign o	disorder	conditio	example	metapla	Preferre	autoimn	rheumat	lupus er	sclerosis	below),	(e.g., as	boosting	immune	suppres	immune	preferre	inflamn	inflamn
	invention (including announces and agonists or antagonists of	the invention) to regulate	STAT transcription factors and	modulate gene expression	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.
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Highly preferred indications include blood disorders (e.g.,	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,
Exemplary human T cells, such as the SUPT cell line, that	may be used according to utese assays are publicly available	(e.g., through the ATCC).																										
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HMSKC04	1295	Activation of transcription through NFAT response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of	diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.  Highly preferred indications include blood disorders (e.g., as described below under "Tmmune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").  Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An
			polypeptides of the invention (including antibodies and	additional highly preferred indication is infection (e.g., an
			agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	infectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., leukemia,

		216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	lymphoma, and/or as described below under
		85:6342-6346 (1988); Serfling	"Hyperproliferative
		et al., Biochim Biophys Acta	Disorders"). Preferred
		1498(1):1-18 (2000); De Boer	indications include neoplasms
		et al., Int J Biochem Cell Biol	and cancers, such as, for
		31(10):1221-1236 (1999);	example, leukemia, lymphoma,
		Fraser et al., Eur J Immunol	and prostate, breast, lung,
		29(3):838-844 (1999); and	colon, pancreatic, esophageal,
		Yeseen et al., J Biol Chem	stomach, brain, liver and
	-	268(19):14285-14293 (1993),	urinary cancer. Other preferred
		the contents of each of which	indications include benign
		are herein incorporated by	dysproliferative disorders and
		reference in its entirety. T	pre-neoplastic conditions, such
		cells that may be used	as, for example, hyperplasia,
		according to these assays are	metaplasia, and/or dysplasia.
		publicly available (e.g.,	Preferred indications also
		through the ATCC).	include anemia, pancytopenia,
		Exemplary human T cells that	leukopenia, thrombocytopenia,
		may be used according to these	Hodgkin's disease, acute
		assays include the SUPT cell	lymphocytic anemia (ALL),
	-	line, which is a suspension	plasmacytomas, multiple
		culture of IL-2 and IL-4	myeloma, Burkitt's lymphoma,
		responsive T cells.	arthritis, AIDS, granulomatous
-			disease, inflammatory bowel
			disease, sepsis, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted
			organs and tissues,
			hemophilia, hypercoagulation,

					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
	HMSKC04	1295	Activation of	Assays for the activation of	Highly preferred indications
347			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
	-			invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
	1,-			may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
*				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
				66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
	•			216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative

<del> </del>	as,melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	esophageal, stomach, brain.	liver and urinary cancer. Other	preferred indications include	benign dysproliferative		conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	suppression of immune
85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. I cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.														
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					reactions to transplanted
					organs, asthma and allergy.
	HMSKC04	1295	Activation of	Assays for the activation of	A highly preferred
347			transcription	transcription through the	indication is allergy.
			through STAT6	Signal Transducers and	Another highly preferred
	75.007.5		response element in	Activators of Transcription	indication is asthma.
			immune cells (such	(STAT6) response element are	Additional highly preferred
			as T-cells).	well-known in the art and may	indications include
				be used or routinely modified	inflammation and
				to assess the ability of	inflammatory disorders.
				polypeptides of the invention	Preferred indications include
				(including antibodies and	blood disorders (e.g., as
	-			agonists or antagonists of the	described below under
				invention) to regulate STAT6	"Immune Activity", "Blood-
				transcription factors and	Related Disorders", and/or
				modulate the expression of	"Cardiovascular Disorders").
				multiple genes. Exemplary	Preferred indications include
				assays for transcription	autoimmune diseases (e.g.,
				through the STAT6 response	rheumatoid arthritis, systemic
				element that may be used or	lupus erythematosis, multiple
				routinely modified to test	sclerosis and/or as described
				STAT6 response element	below) and
				activity of the polypeptides of	immunodeficiencies (e.g., as
				the invention (including	described below).
				antibodies and agonists or	Preferred indications include
				antagonists of the invention)	neoplastic diseases (e.g.,
				include assays disclosed in	leukemia, lymphoma,
				Berger et al., Gene 66:1-10	melanoma, and/or as described
				(1998); Cullen and Malm,	below under
				Methods in Enzymol 216:362-	"Hyperproliferative
				368 (1992); Henthorn et al.,	Disorders"). Preferred

indications include neoplasms	and cancers, such as, leukemia,		prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, and Lyme Disease.	An additional preferred	indication is infection (e.g., an
Proc Natl Acad Sci USA	85:6342-6346 (1988); Georas	et al., Blood 92(12):4529-4538	(1998); Moffatt et al.,	Transplantation 69(7):1521-	1523 (2000); Curiel et al., Eur	J Immunol 27(8):1982-1987	(1997); and Masuda et al., J	Biol Chem 275(38):29331-	29337 (2000), the contents of	each of which are herein	incorporated by reference in its	entirety. T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the SUPT cell line,	which is a suspension culture	of IL-2 and IL-4 responsive T	cells.									

					infectious disease as described below under "Infectious Disease").
	HMTBI36	1296	Activation of	Assays for the activation of	Highly preferred indications
348			transcription	transcription through the	include asthma, allergy,
			through NFKB	NFKB response element are	hypersensitivity reactions, and
			response element in	well-known in the art and may	inflammation. Preferred
			immune cells (such	be used or routinely modified	indications include infection
			as EOL1 cells).	to assess the ability of	(e.g., an infectious disease as
				polypeptides of the invention	described below under
				(including antibodies and	"Infectious Disease"),
				agonists or antagonists of the	immunological disorders,
				invention) to regulate NFKB	inflammation and
			-	transcription factors and	inflammatory disorders (e.g.,
				modulate expression of	as described below under
				immunomodulatory genes.	"Immune Activity", and
			-	Exemplary assays for	"Blood-Related Disorders").
•				transcription through the	Preferred indications include
				NFKB response element that	autoimmune diseases (e.g.,
•				may be used or rountinely	rheumatoid arthritis, systemic
				modified to test NFKB-	lupus erythematosis, multiple
				response element activity of	sclerosis and/or as described
				polypeptides of the invention	below) and
-				(including antibodies and	immunodeficiencies (e.g., as
_				agonists or antagonists of the	described below).
				invention) include assays	
				disclosed in Berger et al., Gene	
				66:1-10 (1998); Cullen and	
				Malm, Methods in Enzymol	
				216:362-368 (1992); Henthorn	
				et al., Proc Natl Acad Sci USA	

85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	For example, a reporter assay	(which measures increases in	transcription inducible from a	NFkB responsive element in	EOL-1 cells) may link the	NFKB element to a repeorter	gene and binds to the NFKB	transcription factor, which is	upregulated by cytokines and	other factors. Exemplary	immune cells that may be used	according to these assays	include eosinophils such as the	human EOL-1 cell line of	eosinophils. Eosinophils are a	type of immune cell important	in the allergic responses; they	are recruited to tissues and	mediate the inflammtory	response of late stage allergic	reaction. Eol-1 is a human	eosinophil cell line.
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	HMTBI36	1296	Activation of	Kinase assay. Kinase assays,	A highly preferred
348			Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
			PI3 Kinase	assay, for PI3 kinase signal	includes a method for
			Signalling Pathway	transduction that regulate	increasing muscle cell survival
				glucose metabolism and cell	An alternative highly preferred
			-	survivial are well-known in the	embodiment of the invention
				art and may be used or	includes a method for
				routinely modified to assess	decreasing muscle cell
		-		the ability of polypeptides of	survival. A preferred
	<del></del>			the invention (including	embodiment of the invention
				antibodies and agonists or	includes a method for
				antagonists of the invention) to	stimulating muscle cell
				promote or inhibit glucose	proliferation. In a specific
				metabolism and cell survival.	embodiment, skeletal muscle
				Exemplary assays for PI3	cell proliferation is stimulated.
				kinase activity that may be	An alternative highly preferred
	_			used or routinely modified to	embodiment of the invention
				test PI3 kinase-induced activity	includes a method for
				of polypeptides of the	inhibiting muscle cell
				invention (including antibodies	proliferation. In a specific
				and agonists or antagonists of	embodiment, skeletal muscle
				the invention) include assays	cell proliferation is inhibited.
				disclosed in Forrer et al., Biol	A preferred embodiment of
			- 1	Chem 379(8-9):1101-1110	the invention includes a
				(1998); Nikoulina et al.,	method for stimulating muscle
				Diabetes 49(2):263-271	cell differentiation. In a
				(2000); and Schreyer et al.,	specific embodiment, skeletal
				Diabetes 48(8):1662-1666	muscle cell differentiation is
				(1999), the contents of each of	stimulated. An alternative
			-	which are herein incorporated	highly preferred embodiment
				by reference in its entirety.	of the invention includes a

	Rat myoblast cells that may be	method for inhibiting muscle
	used according to these assays	cell differentiation. In a
	are publicly available (e.g.,	specific embodiment, skeletal
	through the ATCC).	muscle cell differentiation is
	Exemplary rat myoblast cells	inhibited. Highly preferred
	that may be used according to	indications include disorders of
	these assays include L6 cells.	the musculoskeletal system.
	L6 is an adherent rat myoblast	Preferred indications include
	cell line, isolated from primary	neoplastic diseases (e.g., as
	cultures of rat thigh muscle,	described below under
	that fuses to form	"Hyperproliferative
	multinucleated myotubes and	Disorders"), endocrine
	striated fibers after culture in	disorders (e.g., as described
	differentiation media.	below under "Endocrine
		Disorders"), neural disorders
		(e.g., as described below under
		"Neural Activity and
		Neurological Diseases"), blood
		disorders (e.g., as described
		below under "Immune
		Activity", "Cardiovascular
-		Disorders", and/or "Blood-
		Related Disorders"), immune
		disorders (e.g., as described
		below under "Immune
		Activity"), and infection (e.g.,
		as described below under
		"Infectious Disease"). A
		highly preferred indication is
		diabetes mellitus. An
		additional highly preferred

indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g,	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),
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	neuropathy, vision impairment
	(e.g., diabetic retinopathy and
	blindness), ulcers and impaired
	wound healing, infections
	(e.g., infectious diseases and
	disorders as described in the
	"Infectious Diseases" section
 _	below, especially of the
	urinary tract and skin), carpal
	tunnel syndrome and
	Dupuytren's contracture).
	An additional highly preferred
	indication is obesity and/or
	complications associated with
	obesity. Additional highly
	preferred indications include
-	weight loss or alternatively,
 	weight gain. Additional
	highly preferred indications are
	complications associated with
 	insulin resistance.
	Additonal highly preferred
	indications are disorders of the
	musculoskeletal system
	including myopathies,
 	muscular dystrophy, and/or as
	described herein.
	Additional highly preferred
	indications include: myopathy,
	atrophy, congestive heart
 _	foilure goodowie minomon

					fibromas concenital
					intioninas, conferman
					cardiovascular abnormalities,
					heart disease, cardiac arrest,
					heart valve disease, and
					vascular disease. Highly
					preferred indications include
					neoplasms and cancer, such as,
					rhabdomyoma,
					rhabdosarcoma, stomach,
					esophageal, prostate, and
					urinary cancer. Preferred
					indications also include breast,
					lung, colon, pancreatic, brain,
					and liver cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as,
					hyperplasia, metaplasia, and/or
		3			dysplasia.
348	HMTBI36	1296	ICAM in OE19		
	HMTBI36	1296	SEAP in		
348		-	Senescence Assay		
	HMUAP70	1297	Activation of	Assays for the activation of	A preferred embodiment of
349			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method

		the invention (including	for stimulating (e.g.,
		dimensional contractions	inomogramy TME clarks
		antibodies and agonists or	increasing) ling alpha
		antagonists of the invention) to	production. Preferred
		regulate the serum response	indications include blood
,		factors and modulate the	disorders (e.g., as described
		expression of genes involved	below under "Immune
		in growth. Exemplary assays	Activity", "Blood-Related
		for transcription through the	Disorders", and/or
		SRE that may be used or	"Cardiovascular Disorders"),
		routinely modified to test SRE	Highly preferred indications
		activity of the polypeptides of	include autoimmune diseases
		the invention (including	(e.g., rheumatoid arthritis,
		antibodies and agonists or	systemic lupus erythematosis,
••••		antagonists of the invention)	Crohn"s disease, multiple
		include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
-		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
_		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and	immune response. Additional
		Black et al., Virus Genes	highly preferred indications
		12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
		herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
		cells that may be used	arthritis. An additional highly
		according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications
		through the ATCC).	include neoplastic diseases
		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,

																											_		
and/or as described below under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immine
may be used according to these assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.																									
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								-																					

					reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
350	HM V BN46	8671	Froduction of IFNgamma using a T cells	If Ngamma FMA1. If Ng plays a central role in the immune system and is considered to be a proinflammatory cytokine. If Ng promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with
				assess the ability of polypeptides of the invention	chronic granulomatosus disease and malignant

	(including antibodies and	osteonorosis and/or as
		decopolosis, and or as
	agonists or antagonists of the	described below under
	invention) to mediate	"Infectious Disease"). Highly
	immunomodulation, regulate	preferred indications include
	inflammatory activities,	autoimmune disease (e.g.,
	modulate TH2 helper cell	rheumatoid arthritis, systemic
	function, and/or mediate	lupus erythematosis, multiple
	humoral or cell-mediated	sclerosis and/or as described
	immunity. Exemplary assays	below), immunodeficiency
	that test for	(e.g., as described below),
	immunomodulatory proteins	boosting a T cell-mediated
	evaluate the production of	immune response, and
	cytokines, such as Interferon	suppressing a T cell-mediated
	gamma (IFNg), and the	immune response. Additional
	activation of T cells. Such	highly preferred indications
	assays that may be used or	include inflammation and
	routinely modified to test	inflammatory disorders.
	immunomodulatory activity of	Additional preferred
	polypeptides of the invention	indications include idiopathic
	(including antibodies and	pulmonary fibrosis. Highly
	agonists or antagonists of the	preferred indications include
	invention) include the assays	neoplastic diseases (e.g.,
	disclosed in Miraglia et al., J	leukemia, lymphoma,
	Biomolecular Screening 4:193-	melanoma, and/or as described
	204 (1999); Rowland et al.,	below under
	"Lymphocytes: a practical	"Hyperproliferative
 -	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); Gonzalez et al., J Clin	indications include neoplasms
	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,

				of of Annu Don Immunol	breast ling colon nancreatic
			,	et al., Allila INCV Illillandi	Olcast, lung, colon, paneleure,
				15:749-795 (1997), and	esopnageal, stomacn, orain,
				Rheumatology (Oxford)	liver and urinary cancer. Other
				38(3):214-20 (1999), the	preferred indications include
	1447			contents of each of which are	benign dysproliferative
				herein incorporated by	disorders and pre-neoplastic
				reference in its entirety.	conditions, such as, for
				Human T cells that may be	example, hyperplasia,
	·			used according to these assays	metaplasia, and/or dysplasia.
		-		may be isolated using	Preferred indications include
				techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
				human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
				CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
				be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
···					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HMVBN46	1298	VEGF in SW480		
350					
351	HMWEB02	1299	Activation of transcription	Assays for the activation of transcription through the	Highly preferred indications include neoplastic diseases
100			4		

	through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
	response element in	Site (GAS) response element	and/or as described below
	immune cells (such	are well-known in the art and	under "Hyperproliferative
	as T-cells).	may be used or routinely	Disorders"). Highly preferred
		modified to assess the ability	indications include neoplasms
		of polypeptides of the	and cancers, such as, for
		invention (including antibodies	example, leukemia, lymphoma
-		and agonists or antagonists of	(e.g., T cell lymphoma,
		the invention) to regulate	Burkitt's lymphoma, non-
		STAT transcription factors and	Hodgkins lymphoma,
		modulate gene expression	Hodgkin"s disease),
		involved in a wide variety of	melanoma, and prostate,
		cell functions. Exemplary	breast, lung, colon, pancreatic,
-		assays for transcription	esophageal, stomach, brain,
		through the GAS response	liver and urinary cancer. Other
		element that may be used or	preferred indications include
		routinely modified to test	benign dysproliferative
		GAS-response element activity	disorders and pre-neoplastic
		of polypeptides of the	conditions, such as, for
-		invention (including antibodies	example, hyperplasia,
		and agonists or antagonists of	metaplasia, and/or dysplasia.
		the invention) include assays	Preferred indications include
- 3		disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
		66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
		Malm, Methods in Enzymol	lupus erythematosis, multiple
		216:362-368 (1992); Henthorn	sclerosis and/or as described
		et al., Proc Natl Acad Sci USA	below), immunodeficiencies
		85:6342-6346 (1988);	(e.g., as described below),
		Matikainen et al., Blood	boosting a T cell-mediated
		93(6):1980-1991 (1999); and	immune response, and
		Henttinen et al., J Immunol	suppressing a T cell-mediated

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	inflammatory disorders. Highly preferred indications	include blood disorders (e.g., as described below under	"Immune Activity", "Blood-	Related Disorders", and/or   "Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	preferred indication is	idiopathic pulmonary fibrosis.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, arthritis,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilis proprietic
155(10):4582-4587 (1995), the contents of each of which are herein incorporated by	reference in its entirety.  Exemplary mouse T cells that	may be used according to these assays are miblicly available	(e.g., through the ATCC).	Exemplary T cells that may be used according to these assays	include the CTLL cell line,	which is a suspension culture	of IL-2 dependent cytotoxic T	cells.																	
			••••																				A		
				i																					

suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.				A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-4 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-4 production. A highly preferred indication includes asthma. A highly preferred indication includes allergy. A highly preferred indication includes rhinitis. Additional highly preferred indications include inflammation and inflammation and inflammation and
				IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cells, modulate immune cells, modulate and/or mediate humoral or
	IgG in Human B cells SAC	IL-12 in Human B cells SAC	IL-13 in HMC	Production of IL-4
	1299	1299	1300	1300
	HMWEB02	HMWEB02	HMWF002	HMWF002
	351	351	352	352

	cell-mediated immunity.	Highly preferred indications
	Exemplary assays that test for	include neoplastic diseases
	immunomodulatory proteins	(e.g., leukemia, lymphoma,
	evaluate the production of	melanoma, and/or as described
	cytokines, such as IL-4, and	below under
	the stimulation of immune	"Hyperproliferative
	cells, such as B cells, T cells,	Disorders"). Preferred
	macrophages and mast cells.	indications include neoplasms
	Such assays that may be used	and cancers, such as, for
	or routinely modified to test	example, leukemia, lymphoma,
	immunomodulatory activity of	melanoma, and prostate,
	polypeptides of the invention	breast, lung, colon, pancreatic,
	(including antibodies and	esophageal, stomach, brain,
 -	agonists or antagonists of the	liver and urinary cancer. Other
	invention) include the assays	preferred indications include
	disclosed in Miraglia et al., J	benign dysproliferative
	Biomolecular Screening 4:193-	disorders and pre-neoplastic
	204 (1999); Rowland et al.,	conditions, such as, for
	"Lymphocytes: a practical	example, hyperplasia,
	approach" Chapter 6:138-160	metaplasia, and/or dysplasia.
	(2000); Gonzalez et al., J Clin	Preferred indications include
	Lab Anal 8(5):277-283 (1194);	blood disorders (e.g., as
	Yssel et al., Res Immunol	described below under
	144(8):610-616 (1993); Bagley	"Immune Activity", "Blood-
	et al., Nat Immunol 1(3):257-	Related Disorders", and/or
	261 (2000); and van der Graaff	"Cardiovascular Disorders").
	et al., Rheumatology (Oxford)	Preferred indications include
	38(3):214-220 (1999), the	autoimmune diseases (e.g.,
 	contents of each of which are	rheumatoid arthritis, systemic
 	herein incorporated by	lupus erythematosis, multiple
	reference in its entirety.	sclerosis and/or as described

			Human T cells that may be	below) and
			used according to these assays may be isolated using	described below). Preferred
-			techniques disclosed herein or	indications include anemia,
			otherwise known in the art.	pancytopenia, leukopenia,
			Human T cells are primary	thrombocytopenia, Hodgkin's
			human lymphocytes that	disease, acute lymphocytic
			mature in the thymus and	anemia (ALL),
			express a T cell receptor and	plasmacytomas, multiple
<del></del> -			CD3, CD4, or CD8. These	myeloma, Burkitt's lymphoma,
•			cells mediate humoral or cell-	arthritis, AIDS, granulomatous
			mediated immunity and may	disease, inflammatory bowel
			be preactivated to enhance	disease, sepsis, neutropenia,
•			responsiveness to	neutrophilia, psoriasis,
			immunomodulatory factors.	suppression of immune
			•	reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
-				diabetes mellitus, endocarditis,
				meningitis, and Lyme Disease.
				An additonal preferred
				indication is infection (e.g., an
				infectious disease as described
				below under "Infectious
				Disease").
HMWGY65	1301	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
)	1	Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
		Signaling Pathway.	transduction that regulate cell	described below under
		· ·	proliferation, activation, or	"Hyperproliferative
			apoptosis are well known in	Disorders"), blood disorders
•			the art and may be used or	(e.g., as described below under

"Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders", and infection	(e.g., an infectious disease as described below under "Infectious Disease"). Highly	preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Additional	highly preferred indications include inflammation and	inflammatory disorders. Highly preferred indications	also include neoplastic diseases (e.g., leukemia,	lymphoma, and/or as described below under	"Hyperproliferative Disorders"), Highly preferred	indications include neoplasms and cancers. such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain.	liver, and urinary cancer. Other
routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or	antagonists of the invention) to promote or inhibit immune cell (e.g. T-cell) proliferation,	activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be	used or routinely modified to test JNK and p38 kinase-induced activity of	polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include the assays	disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110	(1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999);	Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang	and Karin, Nature 410(6824):37-40 (2001): and	Cobb MH, Prog Biophys Mol Biol 71(3-4)·479-500 (1999):	the contents of each of which	are herein incorporated by	cells that may be used
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											,		

preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin"s disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt"s lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	
according to these assays are publicly available (e.g., through the ATCC).  Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its
	Inhibition of squalene synthetase gene transcription.
	1301
	HMWGY65
	353

with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.		Kinase assay. JNK and p38  kinase assays for signal transduction that regulate cell proliferation, activation, or antibodies and agonists or antibodies and p38  A highly preferred embodiment of the invention includes a method for growth. An alternative highly preferred embodiment of the invention (including antibodies and agonists or antibodies and agonists or promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or and n38 kinase-induced kinase-induced A highly preferred antibodies a method for includes a method for prowth. An alternative includes a method for stimulating endothelial cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or and n38 kinase-induced A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. An alternative highly preferred antibodies and agonists or includes a method for inhibit cell proliferation, activation, and apoptosis. Exemplary assays activity that may be used or and n38 kinase-induced A highly preferred embodiment of the invention includes a method for inhibit cell provides a method for includes a method for includes a method for includes a method for stimulating endothelial cell provides a method for inhibit cell provides a method for includes a method for stimulating endothelial cell provides a method for inhibit cell provide
SE S	IFNg in Human T- cell 2B9	Activation of Kin Endothelial Cell kir p38 or JNK tra Signaling Pathway. pro the the the first and
	1301	1301
	HMWGY65	HMWGY65
	353	353

	nn-194 194 1	activity of polypeptides of the	embodiment of the invention
200		invention (including antibodies	includes a method for
		and agonists or antagonists of	stimulating apoptosis of
		the invention) include the	endothelial cells. An
		assays disclosed in Forrer et	alternative highly preferred
		al., Biol Chem 379(8-9):1101-	embodiment of the invention
		1110 (1998); Gupta et al., Exp	includes a method for
		Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
		(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	A.A. Toronto	Soc Symp 64:29-48 (1999);	A highly preferred
	neri in mener	Chang and Karin, Nature	embodiment of the invention
		410(6824):37-40 (2001); and	includes a method for
	*************	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
		Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
		the contents of each of which	alternative highly preferred
	-	are herein incorporated by	embodiment of the invention
Marie Pater		reference in its entirety.	includes a method for
		Endothelial cells that may be	inhibiting (e.g., decreasing) the
- 1.2		used according to these assays	activation of and/or
		are publicly available (e.g.,	inactivating endothelial cells.
		through the ATCC).	A highly preferred
		Exemplary endothelial cells	embodiment of the invention
		that may be used according to	includes a method for
		these assays include human	stimulating angiogenisis. An
		umbilical vein endothelial cells	alternative highly preferred
		(HUVEC), which are	embodiment of the invention
		endothelial cells which line	includes a method for
		venous blood vessels, and are	inhibiting angiogenesis. A
		involved in functions that	highly preferred embodiment
		include, but are not limited to,	of the invention includes a
		angiogenesis, vascular	method for reducing cardiac

hypertrophy. An alternative		of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as
permeability, vascular tone,	and immune cell extravasation.						44.00																							
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well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,
				ar agradan.																-74-3								-		

ischemia reperfusion injury, rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple
									•																	-			

sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	
	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1302
	HNEAC05
	354

		A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related
quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.		Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the
	MCP-1 in HUVEC	Activation of transcription through serum response element in immune cells (such as natural killer cells).
	1302	1302
	HNEAC05	HNEAC05
	354	354

	4	function of growth-related	Disorders", and/or
	36	genes in many cell types.	"Cardiovascular Disorders"),
	<u> </u>	Exemplary assays for	Highly preferred indications
	- <del></del>	transcription through the SRE	include autoimmune diseases
	<u>中</u>	that may be used or routinely	(e.g., rheumatoid arthritis,
 	<u> </u>	modified to test SRE activity	systemic lupus erythematosis,
	0	of the polypeptides of the	Crohn"s disease, multiple
	<u></u>	invention (including antibodies	sclerosis and/or as described
		and agonists or antagonists of	below), immunodeficiencies
	4	the invention) include assays	(e.g., as described below),
	<del>p</del>	disclosed in Berger et al., Gene	boosting a T cell-mediated
	9	66:1-10 (1998); Cullen and	immune response, and
		Malm, Methods in Enzymol	suppressing a T cell-mediated
	2	216:362-368 (1992); Henthorn	immune response. Additional
	<u>e</u>	et al., Proc Natl Acad Sci USA	highly preferred indications
,	<u>**</u>	85:6342-6346 (1988); Benson	include inflammation and
	<u>e</u>	et al., J Immunol 153(9):3862-	inflammatory disorders, and
	<u>~</u>	3873 (1994); and Black et al.,	treating joint damage in
	<u> </u>	Virus Genes 12(2):105-117	patients with rheumatoid
	<u></u>	(1997), the content of each of	arthritis. An additional highly
	<u> </u>	which are herein incorporated	preferred indication is sepsis.
	9	by reference in its entirety. T	Highly preferred indications
	3	cells that may be used	include neoplastic diseases
	8	according to these assays are	(e.g., leukemia, lymphoma,
	d	publicly available (e.g.,	and/or as described below
•	4	through the ATCC).	under "Hyperproliferative
	<u> </u>	Exemplary T cells that may be	Disorders"). Additionally,
	n	used according to these assays	highly preferred indications
 	<u> </u>	include the NK-YT cell line,	include neoplasms and
	8	which is a human natural killer	cancers, such as, for example,
	O	cell line with cytolytic and	leukemia, lymphoma,

melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	
cytotoxic activity.								•••			*********			•																
																			-											_

				is infection (e.g., an infectious
				disease as described below
HNEEB45	1303	Activation of	Assays for the activation of	A highly preferred indication
!	 	transcription	transcription through the	is obesity and/or complications
		through cAMP	cAMP response element are	associated with obesity.
		response element	well-known in the art and may	Additional highly preferred
		(CRE) in pre-	be used or routinely modified	indications include weight loss
	.u	adipocytes.	to assess the ability of	or alternatively, weight gain.
		•	polypeptides of the invention	An additional highly preferred
			(including antibodies and	indication is diabetes mellitus.
			agonists or antagonists of the	An additional highly preferred
			invention) to increase cAMP,	indication is a complication
			regulate CREB transcription	associated with diabetes (e.g.,
			factors, and modulate	diabetic retinopathy, diabetic
			expression of genes involved	nephropathy, kidney disease
			in a wide variety of cell	(e.g., renal failure,
			functions. For example, a	nephropathy and/or other
			3T3-L1/CRE reporter assay	diseases and disorders as
			may be used to identify factors	described in the "Renal
			that activate the cAMP	Disorders" section below),
			signaling pathway. CREB	diabetic neuropathy, nerve
			plays a major role in	disease and nerve damage
			adipogenesis, and is involved	(e.g., due to diabetic
			in differentiation into	neuropathy), blood vessel
			adipocytes. CRE contains the	blockage, heart disease, stroke,
			binding sequence for the	impotence (e.g., due to diabetic
			transcription factor CREB	neuropathy or blood vessel
			(CRE binding protein).	blockage), seizures, mental
			Exemplary assays for	confusion, drowsiness,

		transcription through the	nonketotic hyperglycemic-
		cAMP response element that	hyperosmolar coma,
		may be used or routinely	cardiovascular disease (e.g.,
	-	modified to test cAMP-	heart disease, atherosclerosis,
		response element activity of	microvascular disease,
		polypeptides of the invention	hypertension, stroke, and other
		(including antibodies and	diseases and disorders as
	-	agonists or antagonists of the	described in the
		invention) include assays	"Cardiovascular Disorders"
		disclosed in Berger et al., Gene	section below), dyslipidemia,
		66:1-10 (1998); Cullen and	endocrine disorders (as
		Malm, Methods in Enzymol	described in the "Endocrine
	-	216:362-368 (1992); Henthorn	Disorders" section below),
		et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
		85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
		et al., Mol Cell Biol	blindness), ulcers and impaired
-		20(3):1008-1020 (2000); and	wound healing, and infection
		Klemm et al., J Biol Chem	(e.g., infectious diseases and
		273:917-923 (1998), the	disorders as described in the
		contents of each of which are	"Infectious Diseases" section
		herein incorporated by	below, especially of the
		reference in its entirety. Pre-	urinary tract and skin), carpal
		adipocytes that may be used	tunnel syndrome and
		according to these assays are	Dupuytren's contracture).
	_	publicly available (e.g.,	Additional highly preferred
		through the ATCC) and/or	indications are complications
		may be routinely generated.	associated with insulin
		Exemplary mouse adipocyte	resistance.
		cells that may be used	
		according to these assays	
		include 3T3-L1 cells. 3T3-L1	

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple
is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1303
	HNEEB45
	355

Berger et al., Gene 66:1-10	below), immunodeficiencies
(1998); Cullen and Malm,	(e.g., as described below),
Methods in Enzymol 216:362-	boosting a T cell-mediated
368 (1992); Henthorn et al.,	immune response, and
Proc Natl Acad Sci USA	suppressing a T cell-mediated
85:6342-6346 (1988); and	immune response. Additional
Black et al., Virus Genes	highly preferred indications
12(2):105-117 (1997), the	include inflammation and
content of each of which are	inflammatory disorders, and
herein incorporated by	treating joint damage in
reference in its entirety. T	patients with rheumatoid
cells that may be used	arthritis. An additional highly
according to these assays are	preferred indication is sepsis.
publicly available (e.g.,	Highly preferred indications
through the ATCC).	include neoplastic diseases
Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
may be used according to these	and/or as described below
assays include the CTLL cell	under "Hyperproliferative
line, which is an IL-2	Disorders"). Additionally,
dependent suspension culture	highly preferred indications
of T cells with cytotoxic	include neoplasms and
activity.	cancers, such as, for example,
	leukemia, lymphoma,
	melanoma, glioma (e.g.,
	malignant glioma), solid
····	tumors, and prostate, breast,
	lung, colon, pancreatic,
	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	benign dysproliferative

						disorders and pre-neoplastic
						conditions, such as, for
						example, hyperplasia,
						metaplasia, and/or dysplasia.
						Preferred indications include
						anemia, pancytopenia,
						leukopenia, thrombocytopenia,
		1100				Hodgkin's disease, acute
						lymphocytic anemia (ALL),
						plasmacytomas, multiple
	_					myeloma, Burkitt's lymphoma,
						arthritis, AIDS, granulomatous
						disease, inflammatory bowel
						disease, neutropenia,
						neutrophilia, psoriasis,
21						suppression of immune
47						reactions to transplanted
						organs and tissues,
-						hemophilia, hypercoagulation,
						diabetes mellitus, endocarditis,
						meningitis, Lyme Disease,
						cardiac reperfusion injury, and
						asthma and allergy. An
				;		additional preferred indication
<del></del>	,					is infection (e.g., an infectious
						disease as described below
						under "Infectious Disease").
		HNEEB45	1303	Activation of	Assays for the activation of	Highly preferred indications
	355			transcription	transcription through the	include asthma, allergy,
				through NFKB	NFKB response element are	hypersensitivity reactions, and
				response element in	well-known in the art and may	inflammation. Preferred

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indications include infection	(e.g., an infectious disease as	described below under	"Infectious Disease"),	immunological disorders,	inflammation and	inflammatory disorders (e.g.,	as described below under	"Immune Activity", and	"Blood-Related Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below).													
be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997);	Aramburau et al., J Exp Med	82(3):801-810 (1995); and	Fraser et al., 29(3):838-844	(1999), the contents of each of
immune cells (such	as EOL1 cells).																													
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t a e d	Highly preferred indications  A are well- may be and chronic), restnosis, diffied to atherosclerosis, asthma and allergy. Highly preferred indications include  s and inflammation and
which are herein incorporated by reference in its entirety. For example, a reporter assay (which measures increases in transcription inducible from a NFkB responsive element in EOL-1 cells) may link the NFKB element to a repeorter gene and binds to the NFKB transcription factor, which is upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important in the allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Eol-1 is a human eosinophil cell line.	Production of Assays for measuring expression of VCAM are well-endothelial cells known in the art and may be used or routinely modified to assess the ability of endothelial cells polypeptides of the invention (HUVEC)) (including antibodies and
	HNEEB45 1303 F
	355

				inflammatory responses.	
	HNEEB45	1303	Caspase		
355			(+paclitaxel) in SW480		
	HNFFC43	1304	Regulation of	Assays for the regulation of	A highly preferred indication
356			transcription via	transcription through the	is diabetes mellitus.
	1		DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
		_	adipocytes	to assess the ability of	diabetes (e.g., diabetic
			-	polypeptides of the invention	retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
<del></del>			***	invention) to activate the	nephropathy and/or other
				DMEF1 response element in a	diseases and disorders as
			-	reporter construct (such as that	described in the "Renal
				containing the GLUT4	Disorders" section below),
_				promoter) and to regulate	diabetic neuropathy, nerve
			_	insulin production. The	disease and nerve damage
				DMEF1 response element is	(e.g., due to diabetic
				present in the GLUT4	neuropathy), blood vessel
				promoter and binds to MEF2	blockage, heart disease, stroke,
	_			transcription factor and another	impotence (e.g., due to diabetic
				transcription factor that is	neuropathy or blood vessel
				required for insulin regulation	blockage), seizures, mental
				of Glut4 expression in skeletal	confusion, drowsiness,
				muscle. GLUT4 is the primary	nonketotic hyperglycemic-
				insulin-responsive glucose	hyperosmolar coma,
				transporter in fat and muscle	cardiovascular disease (e.g.,
				tissue. Exemplary assays that	heart disease, atherosclerosis,
				may be used or routinely	microvascular disease,

				ATCC) and/or may be routinely generated.  Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line.  Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	
356	HNFFC43	1304	Proliferation of immune cells (such as the HMC-1 human mast cell line)	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of eosinophil cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp.,	Highly preferred indications include asthma, allergy, mastocytosis (a rare, heterogeneous disorder characterized by excessive accumulation of mast cells, and their proliferation and action in the skin, central nervous system, and other organs). Preferred indications also include hematopoietic and immunological disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), infection (e.g., as described

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below under "Infectious Disease"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus	erythematosis, multiple sclerosis and/or as described below), and	immunodeficiencies (e.g., as described below).													
Madison, WI, USA ) can be used to measure the number of viable cells in culture based on quantitation of the ATP	present which signals the presence of metabolically active cells. Mast cells are	found in connective and mucosal tissues throughout the body. Mast cell activation (via	immunoglobulin E -antigen, promoted by T helper cell type 2 cytokines) is an important	component of allergic disease.  Dysregulation of mast cell	apoptosis may play a role in allergic disease and mast cell	tumor survival. Mast cell lines that may be used according to	these assays are publicly	routinely generated.	Exemplary mast cells that may be used according to these	assays include HMC-1, which	cell line established from the	peripheral blood of a patient	with mast cell leukemia, and	exhibits many characteristics	of immature mast cells.
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	HNFFC43	1304	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
356			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
			-	routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
				antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as
				promote or inhibit immune cell	described below under
				(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
				activation, and apoptosis.	preferred indications include
				Exemplary assays for JNK and	autoimmune diseases (e.g.,
				p38 kinase activity that may be	rheumatoid arthritis, systemic
				used or routinely modified to	lupus erythematosis, multiple
				test JNK and p38 kinase-	sclerosis and/or as described
				induced activity of	below) and
				polypeptides of the invention	immunodeficiencies (e.g., as
				(including antibodies and	described below). Additional
				agonists or antagonists of the	highly preferred indications
				invention) include the assays	include inflammation and
				disclosed in Forrer et al., Biol	inflammatory disorders.
				Chem 379(8-9):1101-1110	Highly preferred indications
				(1998); Gupta et al., Exp Cell	also include neoplastic
				Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
			-	Kyriakis JM, Biochem Soc	lymphoma, and/or as described
				Symp 64:29-48 (1999); Chang	below under
				and Karin, Nature	"Hyperproliferative
				410(6824):37-40 (2001); and	Disorders"). Highly preferred

HNFFC43 1304			
HNFFC43		Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
HNFFC43		the contents of each of which	lymphoma, prostate, breast,
HNFFC43		are herein incorporated by	lung, colon, pancreatic,
HNFFC43		reference in its entirety. T	esophageal, stomach, brain,
HNFFC43		cells that may be used	liver, and urinary cancer. Other
HNFFC43		according to these assays are	preferred indications include
HNFFC43		publicly available (e.g.,	benign dysproliferative
HNFFC43		through the ATCC).	disorders and pre-neoplastic
HNFFC43		Exemplary mouse T cells that	conditions, such as, for
HNFFC43		may be used according to these	example, hyperplasia,
HNFFC43		assays include the CTLL cell	metaplasia, and/or dysplasia.
HNFFC43		line, which is an IL-2	Preferred indications include
HNFFC43		dependent suspension-culture	arthritis, asthma, AIDS,
HNFFC43		cell line with cytotoxic	allergy, anemia, pancytopenia,
HNFFC43		activity.	leukopenia, thrombocytopenia,
HNFFC43			Hodgkin"s disease, acute
HNFFC43			lymphocytic anemia (ALL),
HNFFC43			plasmacytomas, multiple
HNFFC43			myeloma, Burkitt's lymphoma,
HNFFC43			granulomatous disease,
HNFFC43			inflammatory bowel disease,
HNFFC43			sepsis, psoriasis, suppression
HNFFC43			of immune reactions to
HNFFC43			transplanted organs and
HNFFC43			tissues, endocarditis,
HNFFC43			meningitis, and Lyme Disease.
	Regulation of	Assays for the regulation of	A highly preferred
356	transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
	Malic Enzyme in	are well-known in the art and	An additional highly preferred
	adipocytes	may be used or routinely	indication is a complication

	modified to assess the ability	associated with diabetes (e.g.,
	of polypeptides of the	
	invention (including antibodies	
	and agonists or antagonists of	of (e.g., renal failure,
	the invention) to regulate	
	transcription of Malic Enzyme,	
	a key enzyme in lipogenesis.	
	Malic enzyme is involved in	Disorders" section below),
	lipogenesisand its expression is	n is   diabetic neuropathy, nerve
	stimulted by insulin. ME	disease and nerve damage
	promoter contains two direct	t (e.g., due to diabetic
	repeat (DR1)- like elements	
	MEp and MEd identified as	blockage, heart disease, stroke,
	putative PPAR response	impotence (e.g., due to diabetic
	elements. ME promoter may	y neuropathy or blood vessel
	also responds to AP1 and other	her   blockage), seizures, mental
	transcription factors.	confusion, drowsiness,
	Exemplary assays that may be	be nonketotic hyperglycemic-
	used or routinely modified to	o hyperosmolar coma,
	test for regulation of	cardiovascular disease (e.g.,
	transcription of Malic Enzyme	me heart disease, atherosclerosis,
	(in adipoocytes) by	microvascular disease,
	polypeptides of the invention	n hypertension, stroke, and other
-	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	
	invention) include assays	"Cardiovascular Disorders"
-	disclosed in: Streeper, R.S., et	et   section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	
	Endocrinol, 8(10):1361-9	neuropathy, vision impairment

				(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
				Biol Chem, 274(25):17997-	blindness), ulcers and impaired
				8004 (1999); Ijpenberg, A., et	wound healing, and infection
				al., J Biol Chem,	(e.g., infectious diseases and
				272(32):20108-20117 (1997);	disorders as described in the
				Berger, et al., Gene 66:1-10	"Infectious Diseases" section
				(1988); and, Cullen, B., et al.,	below, especially of the
_				Methods in Enzymol.	urinary tract and skin), carpal
				216:362–368 (1992), the	tunnel syndrome and
				contents of each of which is	Dupuytren's contracture).
				herein incorporated by	An additional highly preferred
				reference in its entirety.	indication is obesity and/or
				Hepatocytes that may be used	complications associated with
				according to these assays are	obesity. Additional highly
				publicly available (e.g.,	preferred indications include
				through the ATCC) and/or	weight loss or alternatively,
	· ·			may be routinely generated.	weight gain. Aditional
				Exemplary hepatocytes that	highly preferred indications are
				may be used according to these	complications associated with
				assays includes the H4IIE rat	insulin resistance.
				liver hepatoma cell line.	
	HNFFC43	1304	SEAP in		
356			Senescence Assay		
Į.	HNFIU96	1305	Activation of	This reporter assay measures	Highly preferred indications
35/			transcription	activation of the NFA1	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
	_	,		cytokine and chemokine	"Infectious Disease"), and
		-		production. Assays for the	inflammation and

			activation of transcription	inflammatory disorders.
			through the Nuclear Factor of	Preferred indications also
			Activated T cells (NFAT)	include blood disorders (e.g.,
			response element are well-	as described below under
			known in the art and may be	"Immune Activity", "Blood-
			used or routinely modified to	Related Disorders", and/or
			assess the ability of	"Cardiovascular Disorders").
			polypeptides of the invention	Preferred indications include
			(including antibodies and	autoimmune diseases (e.g.,
			agonists or antagonists of the	rheumatoid arthritis, systemic
			invention) to regulate NFAT	lupus erythematosis, multiple
	_		transcription factors and	sclerosis and/or as described
	• • • • • • • • • • • • • • • • • • • •		modulate expression of genes	below) and
	-		involved in	immunodeficiencies (e.g., as
			immunomodulatory functions.	described below). Preferred
			Exemplary assays for	indications include neoplastic
			transcription through the	diseases (e.g., leukemia,
			NFAT response element that	lymphoma, melanoma,
			may be used or routinely	prostate, breast, lung, colon,
			modified to test NFAT-	pancreatic, esophageal,
			response element activity of	stomach, brain, liver, and
			polypeptides of the invention	urinary tract cancers and/or as
			(including antibodies and	described below under
			agonists or antagonists of the	"Hyperproliferative
			invention) include assays	Disorders"). Other preferred
		-	disclosed in Berger et al., Gene	indications include benign
			66:1-10 (1998); Cullen and	dysproliferative disorders and
·			Malm, Methods in Enzymol	pre-neoplastic conditions, such
-			216:362-368 (1992); Henthorn	as, for example, hyperplasia,
			et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	ļ		85:6342-6346 (1988); De Boer	Preferred indications include

				et al., Int J Biochem Cell Biol	anemia, pancytopenia,
				31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
				et al., J Immunol	leukemias, Hodgkin's disease,
				165(12):7215-7223 (2000);	acute lymphocytic anemia
				Hutchinson and McCloskey, J	(ALL), plasmacytomas,
				Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
			-	that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HNFJF07	1306	Regulation of	Assays for the regulation of	A highly preferred indication
358			transcription via	transcription through the	is diabetes mellitus.
			DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
			adipocytes	to assess the ability of	diabetes (e.g., diabetic

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retinopathy, diabetic nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and
polypeptides of the invention (including antibodies and	agonists or antagonists of the	invention) to activate the	DMEF1 response element in a	reporter construct (such as that	containing the GLUT4	promoter) and to regulate	insulin production. The	DMEF1 response element is	present in the GLUT4	promoter and binds to MEF2	transcription factor and another	transcription factor that is	required for insulin regulation	of Glut4 expression in skeletal	muscle. GLUT4 is the primary	insulin-responsive glucose	transporter in fat and muscle	tissue. Exemplary assays that	may be used or routinely	modified to test for DMEF1	response element activity (in	adipocytes and pre-adipocytes)	by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed inThai, M.V., et al., J	Biol Chem, 273(23):14285-92	(1998): Mora. S., et al., J Biol
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				clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation culture conditions.	
358	HNFJF07	1306	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypentides of the	A highly preferred indication is diabetes mellitus. An additional highly preferred indication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g.
				invention (including antibodies and agonists or antagonists of	heart disease, atherosclerosis, microvascular disease,

			the invention) include assays	hypertension, stroke, and other
			disclosed in: Friedrichsen BN,	diseases and disorders as
			et al., Mol Endocrinol,	described in the
			15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
			MA, et al., Endocrinology,	section below), dyslipidemia,
			139(4):1494-9 (1998); Hugl	endocrine disorders (as
			SR, et al., J Biol Chem 1998	described in the "Endocrine
			Jul 10;273(28):17771-9	Disorders" section below),
			(1998), the contents of each of	neuropathy, vision impairment
			which is herein incorporated	(e.g., diabetic retinopathy and
			by reference in its entirety.	blindness), ulcers and impaired
			Pancreatic cells that may be	wound healing, and infection
			used according to these assays	(e.g., infectious diseases and
			are publicly available (e.g.,	disorders as described in the
			through the ATCC) and/or	"Infectious Diseases" section
		-14	may be routinely generated.	below, especially of the
			Exemplary pancreatic cells that	urinary tract and skin), carpal
-			may be used according to these	tunnel syndrome and
			assays include rat INS-1 cells.	Dupuytren's contracture). An
			INS-1 cells are a semi-	additional highly preferred
<del></del>			adherent cell line established	indication is obesity and/or
			from cells isolated from an X-	complications associated with
			ray induced rat transplantable	obesity. Additional highly
			insulinoma. These cells retain	preferred indications include
			characteristics typical of native	weight loss or alternatively,
			pancreatic beta cells including	weight gain. Additional highly
			glucose inducible insulin	preferred indications are
			secretion. References: Asfari	complications associated with
			et al. Endocrinology 1992	insulin resistance.
			130:167.	
HNFJF07	1306	Activation of	Assays for the activation of	A preferred embodiment of

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the invention includes a	method for inhibiting (e.g.,	reducing) TNF alpha	production. An alternative	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in
transcription through the	Serum Response Element	(SRE) are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by
transcription	through serum	response element in	immune cells (such	as T-cells).			- 40	-																				***		
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358															_					_						_				

patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and	cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple
reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic	activity.		

					myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease.").
358	HNFJF07	1306	Stimulation of insulin secretion from pancreatic beta cells.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage

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(e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dumiytren's contracture).
upregulated by glucose and also by certain	proteins/peptides, and disregulation is a key	component in diabetes.	Exemplary assays that may be	used or routinely modified to	test for stimulation of insulin	secretion (from pancreatic	cells) by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Ahren, B., et al.,	Am J Physiol, 277(4 Pt	2):R959-66 (1999); Li, M., et	al., Endocrinology,	138(9):3735-40 (1997); Kim,	K.H., et al., FEBS Lett,	377(2):237-9 (1995); and,	Miraglia S et. al., Journal of	Biomolecular Screening,	4:193-204 (1999), the contents	of each of which is herein	incorporated by reference in its	entirety. Pancreatic cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC)	and/or may be routinely	generated Exemulary
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HNFJH45 1307 Activation of transcription through AP1 response element immune cells (sue as T-cells).		pancreatic cells that may be	An additional highly preferred
HNFJH45 1307		used according to these assays	indication is obesity and/or
HNFJH45 1307		include rat INS-1 cells. INS-1	complications associated with
HNFJH45 1307		cells are a semi-adherent cell	obesity. Additional highly
HNFJH45 1307		line established from cells	preferred indications include
HNFJH45 1307		isolated from an X-ray induced	weight loss or alternatively,
HNFJH45 1307		rat transplantable insulinoma.	weight gain. Aditional
HNFJH45 1307		These cells retain	highly preferred indications are
HNFJH45 1307		characteristics typical of native	complications associated with
HNFJH45 1307		pancreatic beta cells including	insulin resistance.
HNFJH45 1307		glucose inducible insulin	
HNFJH45 1307		secretion. References: Asfari	
HNFJH45 1307		et al. Endocrinology 1992	
HNFJH45 1307		130:167.	
		Assays for the activation of	Preferred indications
through AP1 response element immune cells (such as T-cells).	transcription	transcription through the AP1	include neoplastic diseases
response element immune cells (sur as T-cells).	through AP1	response element are known in	(e.g., as described below under
immune cells (su as T-cells).	response element in	the art and may be used or	"Hyperproliferative
as T-cells).	immune cells (such	routinely modified to assess	Disorders"), blood disorders
	as T-cells).	the ability of polypeptides of	(e.g., as described below under
		the invention (including	"Immune Activity",
	***	antibodies and agonists or	"Cardiovascular Disorders",
		antagonists of the invention) to	and/or "Blood-Related
		modulate growth and other cell	Disorders"), and infection
		functions. Exemplary assays	(e.g., an infectious disease as
		for transcription through the	described below under
		AP1 response element that	"Infectious Disease"). Highly
		may be used or routinely	preferred indications include
		modified to test AP1-response	autoimmune diseases (e.g.,
		element activity of	rheumatoid arthritis, systemic
		polypeptides of the invention	lupus erythematosis, multiple

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sclerosis and/or as described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	arthritis, asthma, AIDS,	allergy, anemia, pancytopenia,	leukopenia, thrombocytopenia,	Lodalin's disease agute
(including antibodies and agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1988); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Rellahan et al., J Biol Chem	272(49):30806-30811 (1997);	Chang et al., Mol Cell Biol	18(9):4986-4993 (1998); and	Fraser et al., Eur J Immunol	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension-culture	cell line with cytotoxic	activity.		
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lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	Activation of This reporter assay measures transcription activation of the GATA-3 through GATA-3 signaling pathway in HMC-1 response element in human mast cells line.  as mast cells, cells has been linked to cells has been linked to production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including regulate GATA3 transcription regulate gatos and modulate regulate gatos and modulate regulate gatos and modulate regulate gatos are required to assess regulate gatos and modulate regulate gatos and modulate regulate gatos are required to asses regulate gatos and modulate regulate gatos and modulate regulate gatos are required to asses regulate gatos and modulate regulate gatos are required to asses regulate gatos and modulate regulate gatos are required to asses regulate gatos and modulate regulate gatos are required and modulate regulate gatos are required and agonists or regulate gatos and modulate regulate gatos are required and agonists or required and modulate regulate gatos are required and modulate regulate gatos are required and agonists or required and modulate gatos are required and agonists or r	avaragion of mast cell genes   selection as described
	transcription transcription through GA response ele immune cell as mast cell	
	HNFJH45	_
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		development Exemplary	immunodeficiencies (e.g., as
		secare for transcription	described helow) Preferred
		assays for transcription	described below): received
		through the GAIA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
· •		routinely modified to test	lymphoma, melanoma,
	•••	GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
-		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
_		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
		(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
11.		Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
		Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
		14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
		contents of each of which are	lymphoma, arthritis, AIDS,
		herein incorporated by	granulomatous disease,
		reference in its entirety. Mast	inflammatory bowel disease,
		cells that may be used	sepsis, neutropenia,
		according to these assays are	neutrophilia, psoriasis,
	10-340	publicly available (e.g.,	suppression of immune
		through the ATCC).	reactions to transplanted

ls organs and tissues, hemophilia, hypercoagulation, diabetes and litus, endocarditis, meningitis, and Lyme Disease. line t	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders.  Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").  Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes
	Activation of transcription through NFAT response element in immune cells (such as mast cells).
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			involved in	immunodeficiencies (e.g., as
			immunomodulatory functions.	described below). Preferred
			Exemplary assays for	indications include neoplastic
	<u> </u>		transcription through the	diseases (e.g., leukemia,
			NFAT response element that	lymphoma, melanoma,
			may be used or routinely	prostate, breast, lung, colon,
	-		modified to test NFAT-	pancreatic, esophageal,
			response element activity of	stomach, brain, liver, and
			polypeptides of the invention	urinary tract cancers and/or as
			(including antibodies and	described below under
			agonists or antagonists of the	"Hyperproliferative
			invention) include assays	Disorders"). Other preferred
	£;		disclosed in Berger et al., Gene	indications include benign
			66:1-10 (1998); Cullen and	dysproliferative disorders and
			Malm, Methods in Enzymol	pre-neoplastic conditions, such
		_	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
			et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
			85:6342-6346 (1988); De Boer	Preferred indications include
			et al., Int J Biochem Cell Biol	anemia, pancytopenia,
			31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	•		et al., J Immunol	leukemias, Hodgkin's disease,
			165(12):7215-7223 (2000);	acute lymphocytic anemia
•			Hutchinson and McCloskey, J	(ALL), plasmacytomas,
			Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
			16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
			al., J Exp Med 188:527-537	granulomatous disease,
			(1998), the contents of each of	inflammatory bowel disease,
	•		which are herein incorporated	sepsis, neutropenia,
			by reference in its entirety.	neutrophilia, psoriasis,
			Mast cells that may be used	suppression of immune
			according to these assays are	reactions to transplanted

organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation.
publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase
	Endothelial Cell Apoptosis
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includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred	embodiment of the invention includes a method for inhibiting (e.g., decreasing)	apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for	stimulating angiogenisis. An alternative highly preferred	includes a method for inhibiting angiogenesis	highly preferred embodiment of the invention includes a	method for reducing cardiac hypertrophy. An alternative	nignty preferred embodiment of the invention includes a method for inducing cardiac	hypertrophy. Highly preferred indications include	neoplastic diseases (e.g., as described below under	"Hyperproliterative Disorders"), and disorders of	the cardiovascular system
apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include the assays disclosed in Lee et al., FEBS Lett 485(2-3): 122-126 (2000);	Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996):	the contents of each of which are herein incorporated by	Endothelial cells that may be used according to these assays	are publicly available (e.g., through commercial sources).	Exemplary endothelial cells that may be used according to	unese assays include bovine aortic endothelial cells (bAEC), which are an example	of endothelial cells which line blood vessels and are involved	are not limited to,	angrogenesis, vascular permeability, vascular tone,	and immune cell extravasation.
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heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity
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to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangiopericytoma, lymphangiopericytoma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysmoliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory

vasculitides. Revnaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis sexual disorders
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age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,	inflammatory bowel disease	and Crohn's disease), and pain	management.
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A preferred embodiment of the invention includes a method for inhibiting (e.g.,	reducing) 1NF alpha production. An alternative preferred embodiment of the invention includes a method	for stimulating (e.g., increasing) TNF alpha production. Preferred	disorders (e.g., as described below under "Immune	Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"), Highly preferred indications	include autoimmune diseases	systemic lupus erythematosis,	sclerosis and/or as described	below), immunodeficiencies	boosting a T cell-mediated	immune response, and	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and
Assays for the activation of transcription through the Serum Response Element	(SRE) are well-known in the art and may be used or routinely modified to assess the ability of nolynewides of	the invention (including antibodies and agonists or antagonists of the invention) to	regulate the serum response factors and modulate the expression of genes involved	in growth. Exemplary assays for transcription through the	SRE that may be used or routinely modified to test SRE	activity of the polypeptides of	antibodies and agonists or	anagomists of the myenton) include assays disclosed in	Berger et al., Gene 66:1-10	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are
Activation of transcription through serum	response element in immune cells (such as T-cells).									<del></del>					
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treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications	include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications	cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia,	Hodgkin's disease, acute lymphocytic anemia (ALL),
herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g.,	through the ATCC).  Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with extension	of I cells with cytotoxic activity.	
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					plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
361	HNGAP93	1309	IFNg in Human T-cell 2B9		
361	HNGAP93	1309	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke

expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Activation of Assays for the activation of transcription through the the invention in the as natural killer as natural killer routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the  A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. An alternative of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. An alternative the ability of polypeptides of the invention includes a method for stimulating (e.g., increasing) TNF alpha antibodies and agonists or antibodies and agonists or antibodies and agonists or antibodies and agonists of the invention) to regulate serum response factors and modulate the
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		in growth and upregulate the	Activity", "Blood-Related
		function of growth-related	Disorders", and/or
		genes in many cell types.	"Cardiovascular Disorders"),
		Exemplary assays for	Highly preferred indications
	-	transcription through the SRE	include autoimmune diseases
		that may be used or routinely	(e.g., rheumatoid arthritis,
	_	modified to test SRE activity	systemic lupus erythematosis,
		of the polypeptides of the	Crohn"s disease, multiple
		invention (including antibodies	sclerosis and/or as described
	-	and agonists or antagonists of	below), immunodeficiencies
		the invention) include assays	(e.g., as described below),
		disclosed in Berger et al., Gene	boosting a T cell-mediated
		66:1-10 (1998); Cullen and	immune response, and
		Malm, Methods in Enzymol	suppressing a T cell-mediated
-		216:362-368 (1992); Henthorn	immune response. Additional
		et al., Proc Natl Acad Sci USA	highly preferred indications
	-	85:6342-6346 (1988); Benson	include inflammation and
		et al., J Immunol 153(9):3862-	inflammatory disorders, and
		3873 (1994); and Black et al.,	treating joint damage in
		Virus Genes 12(2):105-117	patients with rheumatoid
		(1997), the content of each of	arthritis. An additional highly
		which are herein incorporated	preferred indication is sepsis.
		by reference in its entirety. T	Highly preferred indications
		cells that may be used	include neoplastic diseases
		according to these assays are	(e.g., leukemia, lymphoma,
		publicly available (e.g.,	and/or as described below
	-	through the ATCC).	under "Hyperproliferative
		Exemplary T cells that may be	Disorders"). Additionally,
		used according to these assays	highly preferred indications
		include the NK-YT cell line,	include neoplasms and
!		which is a human natural killer	cancers, such as, for example,

			cell line with cytolytic and	leukemia, lymphoma,
		-	evtotoxic activity.	melanoma, glioma (e.g.,
				malignant glioma), solid
		-		tumors, and prostate, breast,
	-		440	lung, colon, pancreatic,
		•		esophageal, stomach, brain,
				liver and urinary cancer. Other
				preferred indications include
-				benign dysproliferative
				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
				Preferred indications include
				anemia, pancytopenia,
				leukopenia, thrombocytopenia,
				Hodgkin's disease, acute
				lymphocytic anemia (ALL),
	•			plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
		•		disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
	11			reactions to transplanted
				organs and tissues, hemophilia,
				hypercoagulation, diabetes
				mellitus, endocarditis,
				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
		-		

					asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
363	HNGBT31	1311	TNFa in Human T-cell 2B9		
363	HNGBT31	1311	Activation of	Assays for the activation of	Highly preferred indications
203			through NFKB	transcription unrougn me NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
				transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
			17.00	disclosed in Berger et al., Gene	include neoplastic diseases

		66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
		et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
		al., Virus Gnes 15(2):105-117	indications include neoplasms
		(1997); and Fraser et al.,	and cancers, such as, for
		29(3):838-844 (1999), the	example, melanoma, renal cell
		contents of each of which are	carcinoma, leukemia,
		herein incorporated by	lymphoma, and prostate,
		reference in its entirety.	breast, lung, colon, pancreatic,
		Exemplary human T cells,	esophageal, stomach, brain,
		such as the MOLT4, that may	liver and urinary cancer. Other
		be used according to these	preferred indications include
		assays are publicly available	benign dysproliferative
		(e.g., through the ATCC).	disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications also
			include anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			Hodgkin's disease, acute
			lymphocytic anemia (ALL),
			plasmacytomas, multiple
	-		myeloma, Burkitt's lymphoma,
			arthritis, AIDS, granulomatous
			disease, inflammatory bowel
1911			disease, sepsis, neutropenia,
			neutrophilia, psoriasis,
			hemophilia, hypercoagulation,

					diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.
364	HNGDG40	1312	Proliferation of preadipose cells (such as 3T3-L1 cells)	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of	

	HNGDG40	1312	Activation of Endothelial Cell	through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.  Kinase assay. JNK and p38 kinase assays for signal	A highly preferred	
364			Endothelial Cell p38 or JNK Signaling Pathway.	kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or	embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a	
				routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et	endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred	

al.,	al., Biol Chem 379(8-9):1101-	embodiment of the invention
111	1110 (1998); Gupta et al., Exp	includes a method for
Cell	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
(199	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
Soc	Soc Symp 64:29-48 (1999);	A highly preferred
Cha	Chang and Karin, Nature	embodiment of the invention
410	410(6824):37-40 (2001); and	includes a method for
Cob	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
Biol	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
the	the contents of each of which	alternative highly preferred
are	are herein incorporated by	embodiment of the invention
refe	reference in its entirety.	includes a method for
End	Endothelial cells that may be	inhibiting (e.g., decreasing) the
pesn	used according to these assays	activation of and/or
are	are publicly available (e.g.,	inactivating endothelial cells.
thro	through the ATCC).	A highly preferred
Exe	Exemplary endothelial cells	embodiment of the invention
that	that may be used according to	includes a method for
thes	these assays include human	stimulating angiogenisis. An
quin	umbilical vein endothelial cells	alternative highly preferred
DH)	(HUVEC), which are	embodiment of the invention
endc	endothelial cells which line	includes a method for
vend	venous blood vessels, and are	inhibiting angiogenesis. A
invo	involved in functions that	highly preferred embodiment
incl	include, but are not limited to,	of the invention includes a
angi	angiogenesis, vascular	method for reducing cardiac
pern	permeability, vascular tone,	hypertrophy. An alternative
and	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly

preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative"	Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension.	aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis	and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial	infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Hiohly preferred indications	include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels	such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that

	stimulate angiogenesis and/or
	cardiovascularization. Highly
	preferred are indications that
	inhibit angiogenesis and/or
 	cardiovascularization.
 	Highly preferred indications
	include antiangiogenic activity
	to treat solid tumors,
	leukemias, and Kaposi"s
 	sarcoma, and retinal disorders.
	Highly preferred indications
	include neoplasms and cancer,
	such as, Kaposi"s sarcoma,
	hemangioma (capillary and
	cavernous), glomus tumors,
	telangiectasia, bacillary
	angiomatosis,
	hemangioendothelioma,
	angiosarcoma,
	haemangiopericytoma,
 _	lymphangioma,
	lymphangiosarcoma. Highly
	preferred indications also
	include cancers such as,
 	prostate, breast, lung, colon,
	pancreatic, esophageal,
 	stomach, brain, liver, and
	urinary cancer. Preferred
	indications include benign
	dysproliferative disorders and
	pre-neoplastic conditions, such

as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.
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													-							-										

Additional highly preferred indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include
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					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HNGDJ72	1313	Activation of	Kinase assay. Kinase assays,	A highly preferred
365			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
		-		inhibit cell proliferation,	adipocyte differentiation. An
				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
				kinase activity that may be	includes a method for
				used or routinely modified to	inhibiting adipocyte
	-			test ERK kinase-induced	differentiation. A highly
				activity of polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method
				and agonists or antagonists of	for stimulating (e.g.,
				the invention) include the	increasing) adipocyte
				assays disclosed in Forrer et	activation. An alternative
,				al., Biol Chem 379(8-9):1101-	highly preferred embodiment

			(1999); also include neoplastic f which diseases (e.g., lipomas, d by liposarcomas, and/or as		sse	C). pocyte	ays stroke, impotence and/or as 3T3-L1 described below under				der	he art. and Neurological Diseases"),
1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes	107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang	and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol	Biol /1(3-4):4/9-500 (1999); the contents of each of which are herein incorporated by	reference in its entirety. Mouse adipocyte cells that	may be used according to these assays are publicly available	(e.g., through the ATCC).  Exemplary mouse adipocyte	according to these assays include 3T3-L1 cells. 3T3-L1	is an adherent mouse preadipocyte cell line that is a	continuous substrain of 3T3 fibroblast cells developed	through clonal isolation and undergo a pre-adipocyte to	adipose-like conversion under	conditions known in the art.

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described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the
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"Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below).	neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and	disorders as described in the "Infectious Diseases" section below (particularly of the urinary tract and skin). An additional highly preferred indication is obesity and/or	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with	insulin resistance.  Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred

					indications include.
					hypertension coronary artery
					in periodision, colonary areas
					disease, dyslipidemia,
					gallstones, osteoarthritis,
					degenerative arthritis, eating
					disorders, fibrosis, cachexia,
					and kidney diseases or
					disorders. Preferred
					indications include neoplasms
					and cancer, such as,
					lymphoma, leukemia and
					breast, colon, and kidney
					cancer. Additional preferred
	-				indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HNGDJ72	1313	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
365				by T cells and has strong	embodiment of the invention
		10.00 A-10.00 A-10.00		effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment

		role in mucosal immunity).	of the invention includes a
		IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
		Deregulated expression of IL-6	reducing) IL-6 production. A
		has been linked to autoimmune	highly preferrred indication is
		disease, plasmacytomas,	the stimulation or enhancement
		myelomas, and chronic	of mucosal immunity. Highly
		hyperproliferative diseases.	preferred indications include
		Assays for immunomodulatory	blood disorders (e.g., as
		and differentiation factor	described below under
		proteins produced by a large	"Immune Activity", "Blood-
		variety of cells where the	Related Disorders", and/or
		expression level is strongly	"Cardiovascular Disorders"),
		regulated by cytokines, growth	and infection (e.g., as
		factors, and hormones are well	described below under
		known in the art and may be	"Infectious Disease"). Highly
		used or routinely modified to	preferred indications include
		assess the ability of	autoimmune diseases (e.g.,
		polypeptides of the invention	rheumatoid arthritis, systemic
		(including antibodies and	lupus erythematosis, multiple
		agonists or antagonists of the	sclerosis and/or as described
		invention) to mediate	below) and
		immunomodulation and	immunodeficiencies (e.g., as
		differentiation and modulate T	described below). Highly
		cell proliferation and function.	preferred indications also
		Exemplary assays that test for	include boosting a B cell-
		immunomodulatory proteins	mediated immune response
		evaluate the production of	and alternatively suppressing a
		cytokines, such as IL-6, and	B cell-mediated immune
		the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
j		proliferation and functional	inflammation and

inflammatory disorders.Additional highly preferred indications include asthma and allergy. Highly	preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma,	leukemia, lymphoma, melanoma, and/or as described below under "Hynernrollferative	Disorders"). Highly preferred indications include neoplasms	and cancers, such as, myeloma, plasmacytoma, leukemia,	lymphoma, melanoma, and prostate, breast, lung, colon,		****	dysproliferative disorders and pre-neoplastic conditions, such	as, for example, hyperplasia, metaplasia, and/or dysplasia.	Preferred indications include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	multiple myeloma, Burkitt's
activities. Such assays that may be used or routinely modified to test immunomodulatory and	diffferentiation activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193.	204(1999); Rowland et al., "Lymphocytes: a practical	approach" Chapter 6:138-160 (2000); and Verhasselt et al., J	Immunol 158:2919-2925 (1997), the contents of each of	which are herein incorporated by reference in its entirety.	Human dendritic cells that may be used according to these	assays may be isolated using techniques disclosed herein or	otherwise known in the art. Human dendritic cells are	antigen presenting cells in suspension culture, which.	when activated by antigen	and/or cytokines, initiate and	and functional activities.

lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as
	MIP-lalpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T
	Production of MIP1alpha
	1313
	HNGDJ72
	365

described below under "Immune Activity", "Blood- Related Disorders", and/or "Cardiovascular Disorders").	Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lunus erythematosis.	multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as	described below). Additional highly preferred indications	include inflammation and inflammatory disorders.	Preferred indications also include anemia, pancytopenia,	leukopenia, thrombocytopenia, Hodgkin's disease, acute	lymphocytic anemia (ALL), plasmacytomas, multiple	myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous	disease, inflammatory bowel	neutrophilia, psoriasis,	reactions to transplanted	organs and tissues, hemophilia,	nypercoagulation, diabetes mellitus, endocarditis,
cell differentiation. Exemplary described below under assays that test for immunomodulatory proteins evaluate the production of "Cardiovascular Disor	chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of	monocytes/macrophages and T cells. Such assays that may be used or routinely modified to	test immunomodulatory and chemotaxis activity of	polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays	disclosed in Miraglia et al., J Biomolecular Screening 4:193-	204(1999); Rowland et al., "Lymphocytes: a practical	approach" Chapter 6:138-160 (2000); Satthaporn and	Eremin, J R Coll Surg Ednb 45(1):9-19 (2001): Drakes et	al., Transp Immunol 8(1):17-	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828 (1999), the contents of each of
			W										
							VIII						

				which are herein incorporated	meningitis, Lyme Disease,
				by reference in its entirety.	asthma, and allergy.
				Human dendritic cells that may	Preferred indications also
				be used according to these	include neoplastic diseases
				assays may be isolated using	(e.g., leukemia, lymphoma,
		•		techniques disclosed herein or	and/or as described below
	,			otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
				antigen presenting cells in	indications include neoplasms
				suspension culture, which,	and cancers, such as, leukemia,
				when activated by antigen	lymphoma, prostate, breast,
				and/or cytokines, initiate and	lung, colon, pancreatic,
				upregulate T cell proliferation	esophageal, stomach, brain,
				and functional activities.	liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HNGDJ72	1313	Production of TNF	TNFa FMAT. Assays for	A highly preferred
365			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
				routinely modified to assess	Highly preferred indications

		the ability of polypeptides of	include blood disorders (e.g.,
		the invention (including	as described below under
	-	antibodies and agonists or	"Immune Activity", "Blood-
		antagonists of the invention) to	Related Disorders", and/or
		mediate immunomodulation,	"Cardiovascular Disorders"),
		modulate inflammation and	Highly preferred indications
		cytotoxicity. Exemplary	include autoimmune diseases
	-	assays that test for	(e.g., rheumatoid arthritis,
		immunomodulatory proteins	systemic lupus erythematosis,
		evaluate the production of	Crohn"s disease, multiple
 	•	cytokines such as tumor	sclerosis and/or as described
		necrosis factor alpha (TNFa),	below), immunodeficiencies
		and the induction or inhibition	(e.g., as described below),
-		of an inflammatory or	boosting a T cell-mediated
		cytotoxic response. Such	immune response, and
	***	assays that may be used or	suppressing a T cell-mediated
		routinely modified to test	immune response. Additional
		immunomodulatory activity of	highly preferred indications
		polypeptides of the invention	include inflammation and
		(including antibodies and	inflammatory disorders, and
		agonists or antagonists of the	treating joint damage in
		invention) include assays	patients with rheumatoid
		disclosed in Miraglia et al., J	arthritis. An additional highly
		Biomolecular Screening 4:193-	preferred indication is sepsis.
		204(1999); Rowland et al.,	Highly preferred indications
		"Lymphocytes: a practical	include neoplastic diseases
		approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
-		(2000); Verhasselt et al., Eur J	and/or as described below
		Immunol 28(11):3886-3890	under "Hyperproliferative
		(1198); Dahlen et al., J	Disorders"). Additionally,
		Immunol 160(7):3585-3593	highly preferred indications

include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.o. malionant olioma), solid	tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodekin's disease acuta	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel	disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
(1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828	(1999), the contents of each of which are herein incorporated by reference in its entirety.  Human dendritic cells that may	be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art.  Human dendritic cells are	antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and unremilate T cell proliferation	and functional activities.	
				<del></del>	

				cardiac reperfusion injury, and asthma and allergy. An additional preferred indication
				is infection (e.g., an infectious
				disease as described below
				under "Infectious Disease").
HNGDJ72	1313	Production of	Endothelial cells, which are	Highly preferred indications
		ICAM in	cells that line blood vessels,	include inflammation (acute
		endothelial cells	and are involved in functions	and chronic), restnosis,
		(such as human	that include, but are not limited	atherosclerosis, asthma and
		umbilical vein	to, angiogenesis, vascular	allergy. Highly preferred
		endothelial cells	permeability, vascular tone,	indications include
		(HUVEC))	and immune cell extravasation.	inflammation and
			Exemplary endothelial cells	inflammatory disorders,
			that may be used in ICAM	immunological disorders,
			production assays include	neoplastic disorders (e.g.
-			human umbilical vein	cancer/tumorigenesis), and
			endothelial cells (HUVEC),	cardiovascular disorders (such
			and are available from	as described below under
			commercial sources. The	"Immune Activity", "Blood-
			expression of ICAM (CD54),a	Related Disorders",
			intergral membrane protein,	"Hyperproliferative Disorders"
			can be upregulated by	and/or "Cardiovascular
			cytokines or other factors, and	Disorders"). Highly preferred
			ICAM expression is important	indications include neoplasms
			in mediating immune and	and cancers such as, for
			endothelial cell interactions	example, leukemia, lymphoma,
			leading to immune and	melanoma, renal cell
			inflammatory responses.	carcinoma, and prostate,
			Assays for measuring	breast, lung, colon, pancreatic,
			expression of ICAM-1 are	esophageal, stomach, brain,

	Highly preferred indications include immunological and inflammatory disorders (e.g., such as allergy, asthma, leukemia, etc. and as described below under "Immune Activity", and "Blood-Related to Disorders"). Highly preferred indications also includie
well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety.	Assays measuring production of IL-8 are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate production and/or
	Production of IL-8 by by endothelial cells (such as Human Umbilical Cord Endothelial Cells).
	1313
	HNGDJ72
	365

				secretion of IL-8. For	autoimmune disorders (e.g
				example, FMAT may be used	rheumatoid arthritis, systemic
				or routinely modified to assess	lupus erythematosis, Crohn"s
				the ability of polypeptides of	disease, multiple sclerosis
				the invention (including	and/or as described below),
				antibodies and agonists or	neoplastic disorders (e.g.,
				antagonists of the invention) to	organ cancers such as lung,
				regulate production and/or	liver, colon cancer, and/or as
				secretion of IL-8 from	described below under
				endothelial cells (such as	"Hyperproliferative
				human umbilical vein	Disorders"), and
				endothelial cells (HUVEC)).	cardiovascular disorders (e.g.
				HUVECs are endothelial cells	such as described below under
				which line venous blood	"Cardiovascular Disorders").
				vessels, and are involved in	Preferred indications include
				functions that include, but are	thrombosis, bacteremia and
				not limited to, angiogenesis,	sepsis syndrome and
				vascular permeability, vascular	consequent complications
				tone, and immune cell	(such as acute respiratory
				extravasation. Endothelial	distress syndrome and
				cells play a pivotal role in the	systemic ischemia-reperfusion
				initiation and perpetuation of	resulting from septic shock),
				inflammation and secretion of	restnosis and atherosclerosis.
				L-8 may play an important	
				role in recruitment and	
				activation of immune cells	
		·		such as neutrophils,	
				macrophages, and	
		:		lymphocytes.	
	HNGDJ72	1313	Production of	RANTES FMAT. Assays for	
365			RANTES in	immunomodulatory proteins	

that induce chemotaxis of T	cells, monocytes, and	eosinophils are well known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	induce chemotaxis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical
endothelial cells	(such as human	umbilical vein	endothelial cells	(HUVEC))															199		1		-							
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	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and
approach" Chapter 6:138-160 (2000): Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407 (1995), the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular tone, and immune cell extravasation.	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1313
	HNGDJ72
	365

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inflammatory disorders, immunological disorders, neoplastic disorders (e.g.	cardiovascular disorders (such as described below under	"Immune Activity", "Blood- Related Disorders", "Hyperproliferative Disorders"	and/or "Cardiovascular Disorders"). Highly preferred indications include neoplasms	and cancers such as, for example, leukemia, lymphoma,	melanoma, renal cell carcinoma, and prostate,	breast, lung, colon, pancreatic, esophageal, stomach, brain,	liver and urinary cancer. Other preferred indications include	benign dysproliterative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia.				
agonists or antagonists of the invention) to regulate VCAM expression. For example,	FMAT may be used to meaure the upregulation of cell surface VCAM-1 expresssion in	endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in	functions that include, but are not limited to, angiogenesis, vascular permeability, vascular	tone, and immune cell extravasation. Exemplary	endothelial cells that may be used according to these assays	include human umbilical vein endothelial cells (HUVEC),	which are available from commercial sources. The	expression of VCAM (CD106), a membrane-	associated protein, can be upregulated by cytokines or	other factors, and contributes	to the extravasation of lymphocytes, leucocytes and	other immune cells from blood vessels; thus VCAM	expression plays a role in	promoting immune and
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				inflammatory responses.	
366	HNGDU40	1314	CD152 in Human T cells		
	HNGE029	1315	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
367			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred
				to assess the ability of	indications include immune
	-			polypeptides of the invention	and hematopoietic disorders
				(including antibodies and	(e.g., as described below under
				agonists or antagonists of the	"Immune Activity", and
				invention) to promote or	"Blood-Related Disorders"),
				inhibit cell proliferation,	autoimmune diseases (e.g.,
				activation, and apoptosis.	rheumatoid arthritis, systemic
				Exemplary assays for JNK	lupus erythematosis, Crohn"s
				kinase activity that may be	disease, multiple sclerosis
				used or routinely modified to	and/or as described below),
				test JNK kinase-induced	immunodeficiencies (e.g., as
				activity of polypeptides of the	described below). Highly
				invention (including antibodies	preferred indications also
				and agonists or antagonists of	include boosting or inhibiting
				the invention) include the	immune cell proliferation.
				assays disclosed in Forrer et	Preferred indications include
				al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
				1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
				Cell Res 247(2): 495-504	described below under
				(1999); Kyriakis JM, Biochem	"Hyperproliferative
				Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
				Chang and Karin, Nature	indications include boosting an

eosinophil-mediated immune response, and suppressing an eosinophil-mediated immune response.		
410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety.  Exemplary cells that may be used according to these assays include eosinophils.  Eosinophils are important in the late stage of allergic	reactions; they are recruited to tissues and mediate the inflammatory response of late stage allergic reaction.  Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate	signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38

s" s" d', d', d', l'in ted nits	A preferred embodiment of the invention includes a method for inhibiting (e.g.,	
mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assays for the activation of transcription through the Serum Response Element	
	Activation of transcription through serum	response element in immune cells (such as T-cells)
	1316	
	HNGEP09	
	368	

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(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, biohly preferred indications	ingliny preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,	melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include	benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include	anemia, pancytopeina, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL),	plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel	disease, neutropenia, neutrophilia, psoriasis,
Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2	aependent suspension culture of T cells with cytotoxic activity.							
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suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		
		Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al.,
	HLA-DR in Human T cells	Inhibition of squalene synthetase gene transcription.
	1316	1317
	HNGEP09	HNGHR74
	368	369

980), the herein nce in its				7s for A highly preferred	oteins embodiment of the invention	large   includes a method for	to stimulating (e.g., increasing)			the art embodiment of the invention			MCP-1 production. A highly		nists of   infection (e.g., an infectious		iduce   under "Infectious Disease").	late   Additional highly preferred	i. indications include	test for   inflammation and	oteins inflammatory disorders.	n of cell   Preferred indications include	as   blood disorders (e.g., as	
Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	an T	n T-	an T-	MCP-1 FMAT. Assays for	immunomodulatory proteins	that are produced by a large	variety of cells and act to	induce chemotaxis and	activation of monocytes and T	cells are well known in the art	and may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to mediate	immunomodulation, induce	chemotaxis, and modulate	immune cell activation.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of cell	surface markers, such as	
	CD71 in Human T cells	1317 IFNg in Human T-cell 293T	1317 IL-10 in Human T-cell 293T	1318 Production of	MCP-1	_											No.							
	HNGHR74	HNGHR74	HNGHR74	HNGIH43																				
	369	369	369		370						-													

nrotein (MCP), and the	"Immine Activity" "Blood-
activation of monocutes and T	Related Disorders" and/or
activation of monocytes and 1	Neighbor Disolucis, and/of
cells. Such assays that may be	Cardiovascular Disorders ).
used or routinely modified to	Highly preferred indications
test immunomodulatory and	include autoimmune diseases
 differentiation activity of	(e.g., rheumatoid arthritis,
 polypeptides of the invention	systemic lupus erythematosis,
(including antibodies and	multiple sclerosis and/or as
agonists or antagonists of the	described below) and
invention) include assays	immunodeficiencies (e.g., as
disclosed in Miraglia et al., J	described below). Preferred
Biomolecular Screening 4:193-	indications also include
204(1999); Rowland et al.,	anemia, pancytopenia,
"Lymphocytes: a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	lymphocytic anemia (ALL),
Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
158:2919-2925 (1997), the	disease, inflammatory bowel
 contents of each of which are	disease, sepsis, neutropenia,
herein incorporated by	neutrophilia, psoriasis,
 reference in its entirety.	suppression of immune
Human dendritic cells that may	reactions to transplanted
be used according to these	organs and tissues,
 assays may be isolated using	hemophilia, hypercoagulation,
techniques disclosed herein or	diabetes mellitus, endocarditis,
otherwise known in the art.	meningitis (bacterial and
Human dendritic cells are	viral), Lyme Disease, asthma,
antigen presenting cells in	and allergy Preferred
suspension culture, which,	indications also include

				when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
370	HNGIH43	1318	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of	Highly preferred indications include allergy, asthma, and rhimitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or

the invention (including	"Cardiovascular Disorders").
ontibodies and agonists or	Drafarrad indications include
antidonies and agoinsts of	
 antagonists of the invention) to	autoimmune diseases (e.g.,
 regulate GATA3 transcription	rheumatoid arthritis, systemic
factors and modulate	lupus erythematosis, multiple
expression of mast cell genes	sclerosis and/or as described
important for immune response	
development. Exemplary	immunodeficiencies (e.g., as
assays for transcription	described below). Preferred
through the GATA3 response	indications include neoplastic
element that may be used or	diseases (e.g., leukemia,
routinely modified to test	lymphoma, melanoma,
GATA3-response element	prostate, breast, lung, colon,
activity of polypeptides of the	pancreatic, esophageal,
invention (including antibodies	
and agonists or antagonists of	urinary tract cancers and/or as
the invention) include assays	described below under
disclosed in Berger et al., Gene	e "Hyperproliferative
66:1-10 (1998); Cullen and	Disorders"). Other preferred
Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	dysproliferative disorders and
et al., Proc Natl Acad Sci USA	
85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
Quant Biol 64:563-571 (1999);	; Preferred indications include
Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
Cell 89(4):587-596 (1997); and	
Henderson et al., Mol Cell Biol	I (ALL), plasmacytomas,
14(6):4286-4294 (1994), the	

lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to
	Activation of transcription through NFAT response element in immune cells (such as mast cells).
	1318
	HNGIH43
	370

"Cardiovascular Disorders"). Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's
assess the ability of polypeptides of the invention	(including antibodies and agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali	et al., J Immunol	165(12):7215-7223 (2000);	Hutchinson and McCloskey, J	Biol Chem 270(27):16333-
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				7																								
																											•	

				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
				al., J Exp Med 188:32/-33/ (1998), the contents of each of	granulomatous disease, inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
	444			Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
		-		that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
370	HNGIH43	1318	SEAP in UMR-106		
	HNGIJ31	1319	Activation of	Assays for the activation of	Preferred indications include
371			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described
				agonists or antagonists of the	below under "Infectious
				invention) to increase cAMP	Disease"). Preferred

indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated	immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include neoplastic diseases	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma,	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other
and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of	cell functions. Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element	activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of	which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary mouse T cells that

		modified to assess the ability	inhibiting (e.g., reducing)
		of polypeptides of the	MCP-1 production. A highly
		invention (including antibodies	is
		and agonists or antagonists of	infection (e.g., an infectious
		the invention) to mediate	disease as described below
		immunomodulation, induce	under "Infectious Disease").
		chemotaxis, and modulate	Additional highly preferred
		immune cell activation.	indications include
		Exemplary assays that test for	inflammation and
		immunomodulatory proteins	inflammatory disorders.
		evaluate the production of cell	Preferred indications include
		surface markers, such as	blood disorders (e.g., as
		monocyte chemoattractant	described below under
		protein (MCP), and the	"Immune Activity", "Blood-
		activation of monocytes and T	Related Disorders", and/or
		cells. Such assays that may be	"Cardiovascular Disorders").
		used or routinely modified to	Highly preferred indications
		test immunomodulatory and	include autoimmune diseases
		diffferentiation activity of	(e.g., rheumatoid arthritis,
		polypeptides of the invention	systemic lupus erythematosis,
		(including antibodies and	multiple sclerosis and/or as
		agonists or antagonists of the	described below) and
_		invention) include assays	) S
		disclosed in Miraglia et al., J	described below). Preferred
		Biomolecular Screening 4:193-	indications also include
		204(1999); Rowland et al.,	anemia, pancytopenia,
		"Lymphocytes: a practical	leukopenia, thrombocytopenia,
		approach" Chapter 6:138-160	Hodgkin's disease, acute
		(2000); Satthaporn and	lymphocytic anemia (ALL),
		Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
		45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,

371	insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
	from socionitio	the art and may be used or	An additional highly preferred
	Hom pancicanc	une art and modified to seeses	indication is a complication
	Deta cells.	Tournely mounted to assess	mulcumon is a comprisance.
		the ability of polypeptides of	associated with diabetes (e.g.,
		the invention (including	diabetic retinopathy, diabetic
		antibodies and agonists or	nephropathy, kidney disease
		antagonists of the invention) to	(e.g., renal failure,
		stimulate insulin secretion.	nephropathy and/or other
		For example, insulin secretion	diseases and disorders as
		is measured by FMAT using	described in the "Renal
-	- 47	anti-rat insulin antibodies.	Disorders" section below),
	,	Insulin secretion from	diabetic neuropathy, nerve
		pancreatic beta cells is	disease and nerve damage
		upregulated by glucose and	(e.g., due to diabetic
		also by certain	neuropathy), blood vessel
	-	proteins/peptides, and	blockage, heart disease, stroke,
		disregulation is a key	impotence (e.g., due to diabetic
		component in diabetes.	neuropathy or blood vessel
		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
		test for stimulation of insulin	nonketotic hyperglycemic-
		secretion (from pancreatic	hyperosmolar coma,
	-	cells) by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Ahren, B., et al.,	diseases and disorders as
		Am J Physiol, 277(4 Pt	described in the
		2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
		al., Endocrinology,	section below), dyslipidemia,
-		138(9):3735-40 (1997); Kim,	endocrine disorders (as

				K.H., et al., FEBS Lett,	described in the "Endocrine Disorders" section below)
				377(2):237-9 (1993); and, Miraglia S et. al., Journal of	neuropathy, vision impairment
				Biomolecular Screening,	(e.g., diabetic retinopathy and
				4:193-204 (1999), the contents	blindness), ulcers and impaired
				of each of which is herein	wound healing, and infection
				incorporated by reference in its	(e.g., infectious diseases and
				entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
				assays are publicly available	below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
				pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
-				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HNGIJ31	1319	Activation of	Kinase assay. Kinase assays,	A highly preferred
371			Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
			PI3 Kinase	assay, for PI3 kinase signal	includes a method for
			Signalling Pathway	transduction that regulate	increasing muscle cell survival
			7		

An alternative highly preferred	embodiment of the invention	includes a method for	decreasing muscle cell	survival. A preferred	embodiment of the invention	includes a method for	stimulating muscle cell	proliferation. In a specific	embodiment, skeletal muscle	cell proliferation is stimulated.	An alternative highly preferred	embodiment of the invention	includes a method for	inhibiting muscle cell	proliferation. In a specific	embodiment, skeletal muscle	cell proliferation is inhibited.	A preferred embodiment of	the invention includes a	method for stimulating muscle	cell differentiation. In a	specific embodiment, skeletal	muscle cell differentiation is	stimulated. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting muscle	cell differentiation. In a	specific embodiment, skeletal	muscle cell differentiation is
glucose metabolism and cell	survivial are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	promote or inhibit glucose	metabolism and cell survival.	Exemplary assays for PI3	kinase activity that may be	used or routinely modified to	test PI3 kinase-induced activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Forrer et al., Biol	Chem 379(8-9):1101-1110	(1998); Nikoulina et al.,	Diabetes 49(2):263-271	(2000); and Schreyer et al.,	Diabetes 48(8):1662-1666	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Rat myoblast cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).
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s inhibited. Highly preferred indications include disorders of		st   Preferred indications include	ry neoplastic diseases (e.g., as	described below under	"Hyperproliferative			below under "Endocrine	Disorders"), neural disorders	(e.g., as described below under	"Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus.	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease
Exemplary rat myoblast cells that may be used according to	these assays include L6 cells.	L6 is an adherent rat myoblast	cell line, isolated from primary	cultures of rat thigh muscle,	that fuses to form	multinucleated myotubes and	striated fibers after culture in	differentiation media.															-						
																									Jan Carlotte (1988)				
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(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g,	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infections
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(e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the	urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture).  An additional highly preferred indication is obesity and/or complications associated with	preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	Additional highly preferred indications are disorders of the musculoskeletal system including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest,
	·····		

vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred	lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.	Highly preferred indications include asthma, allergy, hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis
		Kinase assay. JNK kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be
		Activation of JNK Signaling Pathway in immune cells (such as eosinophils).
		1320
		HNGIQ46
		372

used or routinely modified to		and/or as described below).
test JNK kinase-induced	_	immunodeficiencies (e.g., as
activity of polypeptides of the		described below). Highly
invention (including antibodies	S	preferred indications also
and agonists or antagonists of		include boosting or inhibiting
the invention) include the		immune cell proliferation.
assays disclosed in Forrer et		Preferred indications include
al., Biol Chem 379(8-9):1101-		neoplastic diseases (e.g.,
1110 (1998); Gupta et al., Exp		leukemia, lymphoma, and/or as
Cell Res 247(2): 495-504		described below under
(1999); Kyriakis JM, Biochem	<u>·</u>	"Hyperproliferative
Soc Symp 64:29-48 (1999);		Disorders"). Highly preferred
Chang and Karin, Nature		indications include boosting an
410(6824):37-40 (2001); and		eosinophil-mediated immune
Cobb MH, Prog Biophys Mol		response, and suppressing an
Biol 71(3-4):479-500 (1999);		eosinophil-mediated immune
the contents of each of which		response.
are herein incorporated by	ted by	
reference in its entirety.	rety.	
Exemplary cells that may be	t may be	
used according to these assays	nese assays	
include eosinophils.		
Eosinophils are important in	ortant in	
the late stage of allergic	rgic	
reactions; they are recruited to	ecruited to	
tissues and mediate the	the	
inflammatory response of late	nse of late	
stage allergic reaction.	on.	
Moreover, exemplary assays	ry assays	
that may be used or routinely	routinely	
modified to assess the ability	he ability	

of polypeptides of the invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt 1):565-74; and,	Sousa AR, et al., "In vivo	resistance to corticosteroids in	bronchial asthma is associated	with enhanced	phosyphorylation of JUN N-	terminal kinase and failure of	prednisolone to inhibit JUN N-
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				terminal kinase	
				phosphorylation" J Allergy	
			200000000000000000000000000000000000000	Clin Immunol; Sep;104(3 Pt	
				1):565-74 (1999); the contents	
				of each of which are herein	
	-			incorporated by reference in its	
				entirety.	
	HNGJE50	1321	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
373				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
	_			disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
	_			variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
		,		used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic

(including antibodies and	lupus erythematosis, multiple
agonists or antagonists of the	sclerosis and/or as described
invention) to mediate	below) and
immunomodulation and	immunodeficiencies (e.g., as
differentiation and modulate T	described below). Highly
cell proliferation and function.	preferred indications also
Exemplary assays that test for	include boosting a B cell-
immunomodulatory proteins	mediated immune response
evaluate the production of	and alternatively suppressing a
cytokines, such as IL-6, and	B cell-mediated immune
the stimulation and	response. Highly preferred
upregulation of T cell	indications include
proliferation and functional	inflammation and
activities. Such assays that	inflammatory
may be used or routinely	disorders.Additional highly
modified to test	preferred indications include
immunomodulatory and	asthma and allergy. Highly
diffferentiation activity of	preferred indications include
polypeptides of the invention	neoplastic diseases (e.g.,
(including antibodies and	myeloma, plasmacytoma,
agonists or antagonists of the	leukemia, lymphoma,
invention) include assays	melanoma, and/or as described
disclosed in Miraglia et al., J	below under
Biomolecular Screening 4:193-	"Hyperproliferative
204(1999); Rowland et al.,	Disorders"). Highly preferred
"Lymphocytes: a practical	indications include neoplasms
 approach" Chapter 6:138-160	and cancers, such as, myeloma,
(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
Immunol 158:2919-2925	lymphoma, melanoma, and
(1997), the contents of each of	prostate, breast, lung, colon,
which are herein incorporated	pancreatic, esophageal,

				by reference in its entirety.	stomach, brain, liver and
				Human dendritic cells that may	urinary cancer. Other preferred
				be used according to these	indications include benign
				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
		-		antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
	-				reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
	710				Disease").
	HNGJE50	1321	Insulin Secretion	Assays for measuring secretion	A highly preferred indication
373		- [		of insulin are well-known in	is diabetes mellitus. An

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additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic	nephropathy, kidney disease (e.g., renal failure,	diseases and disorders as described in the "Renal	Disorders" section below), diabetic neuropathy, nerve	disease and nerve damage (e.g., due to diabetic	neuropathy), blood vessel	blockage, neart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness, nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine
the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) to	stimulate insulin secretion.  For example, insulin secretion is measured by FMAT using	anti-rat insulin antibodies. Insulin secretion from	pancreatic beta cells is upregulated by glucose and	also by certain	proteins/peptides, and disregulation is a key	component in diabetes.	Exemplary assays that may be	used or routinely modified to test for stimulation of insulin	secretion (from pancreatic	cells) by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in: Shimizu, H., et	al., Endocr J, 47(3):261-9	(2000); Salapatek, A.M., et al.,	Mol Endocrinol, 13(8):1305-	17 (1999); Filipsson, K., et al.,	Ann N Y Acad Sci, 865:441-4
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			(1998): Olson. L.K et al J	Disorders" section below).
-			Biol Chem, 271(28):16544-52	neuropathy, vision impairment
			(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
			Journal of Biomolecular	blindness), ulcers and impaired
			Screening, 4:193-204 (1999),	wound healing, and infection
			the contents of each of which	(e.g., infectious diseases and
			is herein incorporated by	disorders as described in the
			reference in its entirety.	"Infectious Diseases" section
			Pancreatic cells that may be	below, especially of the
			used according to these assays	urinary tract and skin), carpal
			are publicly available (e.g.,	tunnel syndrome and
			through the ATCC) and/or	Dupuytren's contracture).
			may be routinely generated.	An additional highly preferred
		`	Exemplary pancreatic cells that	indication is obesity and/or
			may be used according to these	complications associated with
			assays include HITT15 Cells.	obesity. Additional highly
			HITT15 are an adherent	preferred indications include
			epithelial cell line established	weight loss or alternatively,
			from Syrian hamster islet cells	weight gain. Additional highly
	-		transformed with SV40. These	preferred indications are
			cells express glucagon,	complications associated with
			somatostatin, and	insulin resistance.
			glucocorticoid receptors. The	
			cells secrete insulin, which is	
			stimulated by glucose and	
			glucagon and suppressed by	
			somatostatin or	
			glucocorticoids. ATTC# CRL-	
			1777 Refs: Lord and	
			Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc.	

					A highly preferred embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	TNF alpha production. An	alternative highly preferred	embodiment of the invention	includes a method for	stimulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple
Natl. Acad. Sci. USA 78: 4339-4343, 1981.					TNFa FMAT. Assays for immunomodulatory proteins	produced by activated	macrophages, T cells,	fibroblasts, smooth muscle,	and other cell types that exert a	wide variety of inflammatory	and cytotoxic effects on a	variety of cells are well known	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of
	IgG in Human B cells SAC	TNFa in Human T-cell 293T	IL-10 in Human T-cell 2B9	CXCR4 in SW480	Production of TNF alpha by dendritic	cells		-																
	1321	1321	1321	1321	1322																			
	HNGJE50	HNGJE50	HNGJE50	HNGJE50	HNGJO57																			
	373	373	373	373	374																			

	cvtokines such as tumor	sclerosis and/or as described
	necrosis factor alpha (TNFa),	below), immunodeficiencies
	and the induction or inhibition	(e.g., as described below),
	of an inflammatory or	boosting a T cell-mediated
	cytotoxic response. Such	immune response, and
	 assays that may be used or	suppressing a T cell-mediated
	routinely modified to test	immune response. Additional
	immunomodulatory activity of	highly preferred indications
	polypeptides of the invention	include inflammation and
	 (including antibodies and	inflammatory disorders, and
	agonists or antagonists of the	treating joint damage in
-	invention) include assays	patients with rheumatoid
	disclosed in Miraglia et al., J	arthritis. An additional highly
	Biomolecular Screening 4:193-	preferred indication is sepsis.
	204(1999); Rowland et al.,	Highly preferred indications
	"Lymphocytes: a practical	include neoplastic diseases
	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000); Verhasselt et al., Eur J	and/or as described below
	Immunol 28(11):3886-3890	under "Hyperproliferative
	(1198); Dahlen et al., J	Disorders"). Additionally,
	Immunol 160(7):3585-3593	highly preferred indications
	(1998); Verhasselt et al., J	include neoplasms and
	Immunol 158:2919-2925	cancers, such as, leukemia,
	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
	(1999), the contents of each of	tumors, and prostate, breast,
	 which are herein incorporated	lung, colon, pancreatic,
	by reference in its entirety.	esophageal, stomach, brain,
	Human dendritic cells that may	liver and urinary cancer. Other
	be used according to these	preferred indications include
	assays may be isolated using	benign dysproliferative

				techniques disclosed herein or	disorders and pre-neoplastic
				Unierwise Known in the art.  Human dendritic cells are	example, hyperplasia,
				antigen presenting cells in	metaplasia, and/or dysplasia.
				suspension culture, which,	Preferred indications include
				when activated by antigen	anemia, pancytopenia,
				and/or cytokines, initiate and	leukopenia, thrombocytopenia,
				upregulate T cell proliferation	Hodgkin's disease, acute
				and functional activities.	lymphocytic anemia (ALL),
					plasmacytomas, multiple
<del>.</del>					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
·					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
374	HNGJO57	1322	IFNg in Human T-cell 293T		
375	HNGJP69	1323	SEAP in 293/ISRE		
				- Line	11.

	HNGJP69	1323	Activation of	Assays for the activation of	A highly preferred indication
375			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
				transcription factor CREB	neuropathy or blood vessel
		2.77		(CRE binding protein).	blockage), seizures, mental
				Exemplary assays for	confusion, drowsiness,
	-			transcription through the	nonketotic hyperglycemic-
				cAMP response element that	hyperosmolar coma,
				may be used or routinely	cardiovascular disease (e.g.,
				modified to test cAMP-	heart disease, atherosclerosis,

through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	
	transcription through serum response element in pre-adipocytes.
	375 HNGJP69

				Proc Natl Acad Sci USA	confusion, drowsiness,
				85:6342-6346 (1988); and	nonketotic hyperglycemic-
				Black et al., Virus Genes	hyperosmolar coma,
				12(2):105-117 (1997), the	cardiovascular disease (e.g.,
				content of each of which are	heart disease, atherosclerosis,
				herein incorporated by	microvascular disease,
				reference in its entirety. Pre-	hypertension, stroke, and other
				adipocytes that may be used	diseases and disorders as
				according to these assays are	described in the
				publicly available (e.g.,	"Cardiovascular Disorders"
				through the ATCC) and/or	section below), dyslipidemia,
				may be routinely generated.	endocrine disorders (as
				Exemplary mouse adipocyte	described in the "Endocrine
				cells that may be used	Disorders" section below),
				according to these assays	neuropathy, vision impairment
				include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
				is an adherent mouse	blindness), ulcers and impaired
				preadipocyte cell line that is a	wound healing, and infection
				continuous substrain of 3T3	(e.g., infectious diseases and
				fibroblast cells developed	disorders as described in the
				through clonal isolation and	"Infectious Diseases" section
				undergo a pre-adipocyte to	below). Additional highly
				adipose-like conversion under	preferred indications are
				appropriate differentiation	complications associated with
				conditions known in the art.	insulin resistance.
	HNGJP69	1323	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
375			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.
	-			be used or routinely modified	Additional highly preferred

indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Rlood-Related Disorders").	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis	and/or as described below), immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting or inhibiting	immune cell proliferation.  Preferréd indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative	Disorders"). Highly preferred indications include boosting an eosinophil-mediated immune response, and suppressing an eosinophil-mediated immune response.	
to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or	inhibit cell proliferation, activation, and apoptosis.  Exemplary assays for JNK kinase activity that may be	used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and aconists or antagonists of	the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kvriakis JM. Biochem	Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which	are herein incorporated by reference in its entirety.  Exemplary cells that may be used according to these assays include eosinophils.
		-			

Eosinophils are important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammatory response of late	Moreover, exemplary assays that may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-	terminal kinase and p38 mitogen-activated protein kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J
	·		

				Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and,	
				Sousa AR, et al., "In vivo	
				resistance to corticosteroids in	
				bronchial asthma is associated	
				with enhanced	
				phosyphorylation of JUN N-	
				terminal kinase and failure of	
				prednisolone to inhibit JUN N-	
				terminal kinase	
				phosphorylation" J Allergy	
				Clin Immunol; Sep;104(3 Pt	
				1):565-74 (1999); the contents	
				of each of which are herein	
				incorporated by reference in its	
				entirety.	
	HNGJP69	1323	Activation of	This reporter assay measures	Highly preferred indications
375			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
-17				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
	-11			art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
		·		the invention (including	"Cardiovascular Disorders").

	antagonists of the invention) to autoimmine diseases (e.g.,	-	ll genes	important for immune response   below) and	development. Exemplary immunodeficiencies (e.g., as	assays for transcription described below). Preferred	bonse	element that may be used or diseases (e.g., leukemia,	routinely modified to test   lymphoma, melanoma,	GATA3-response element prostate, breast, lung, colon,	activity of polypeptides of the   pancreatic, esophageal,	S	and agonists or antagonists of urinary tract cancers and/or as	the invention) include assays described below under	disclosed in Berger et al., Gene   "Hyperproliferative	66:1-10 (1998); Cullen and Disorders"). Other preferred	Malm, Methods in Enzymol indications include benign	216:362-368 (1992); Henthorn   dysproliferative disorders and	et al., Proc Natl Acad Sci USA   pre-neoplastic conditions, such	85:6342-6346 (1988); Flavell as, for example, hyperplasia,	et al., Cold Spring Harb Symp   metaplasia, and/or dysplasia.	Quant Biol 64:563-571 (1999);   Preferred indications include	Rodriguez-Palmero et al., Eur   anemia, pancytopenia,	J Immunol 29(12):3914-3924   leukopenia, thrombocytopenia,	(1999); Zheng and Flavell,   leukemias, Hodgkin's disease,	(4):587-596 (1997); and acute lymphocytic anemia	Henderson et al., Mol Cell Biol   (ALL), plasmacytomas,	14(6):4286-4294 (1994), the   multiple myeloma, Burkitt's	contents of each of which are   lymphoma, arthritis, AIDS,
antibodies	antagonis remiate C	factors an	expression	important	developm	assays for	through th	element th	routinely	GATA3-r	activity of	invention	and agoni	the invent	disclosed	66:1-10	Malm, M	216:362-3	et al., Pro	85:6342-6	et al., Col	Quant Bio	Rodrigue:	J Immunc	(1999); Z	Cell 89(4)	Henderso	14(6):428	contents

granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").
herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of
	Activation of transcription through NFAT response element in immune cells (such as mast cells).
	1323
	HNGJP69
	375

Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,
polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali	et al., J Immunol	165(12):7215-7223 (2000);	Hutchinson and McCloskey, J	Biol Chem 270(27):16333-	16338 (1995), and Turner et
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granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications include immunological and hempatopoietic disorders (e.g., as described below under
al., J Exp Med 188:527-537 (1998), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the
	Activation of transcription through NFKB response element in immune cells (such as basophils).
	1323
	HNGJP69
	375

				according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils.	
375	HNGJP69	1323	SEAP in Ku812/NFkB (TNF synergy)		
376	HNGJT54	1324	Activation of transcription	Assays for the activation of	Preferred indications include
2			through cAMP	cAMP response element are	described below under
			response element in immine cells (such	well-known in the art and may	"Immune Activity", "Blood-
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
			-	(including antibodies and	infectious disease as described
				agonists or antagonists of the	Ū.
			-	invention) to increase cAMP	Disease"). Preferred
			,	and regulate CREB	indications include
	-	41		transcription factors, and	autoimmune diseases (e.g.,
				modulate expression of genes	rheumatoid arthritis, systemic
				involved in a wide variety of	lupus erythematosis, multiple
		···		cell functions. Exemplary	sclerosis and/or as described
				assays for transcription	below), immunodeficiencies
				through the cAMP response	(e.g., as described below),
				element that may be used or	boosting a T cell-mediated
				routinely modified to test	immune response, and
				cAMP-response element	suppressing a T cell-mediated

			activity of nolvnentides of the	immune response. Additional
			invention (including antibodies	preferred indications include
			and agonists or antagonists of	inflammation and
			the invention) include assays	inflammatory disorders.
			disclosed in Berger et al., Gene	Highly preferred indications
			66:1-10 (1998); Cullen and	include neoplastic diseases
			Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
			216:362-368 (1992); Henthorn	and/or as described below
			et al., Proc Natl Acad Sci USA	under "Hyperproliferative
			85:6342-6346 (1988); Black et	Disorders"). Highly preferred
			al., Virus Genes 15(2):105-117	indications include neoplasms
			(1997); and Belkowski et al., J	and cancers, such as, for
			Immunol 161(2):659-665	example, leukemia, lymphoma
			(1998), the contents of each of	(e.g., T cell lymphoma,
			which are herein incorporated	Burkitt's lymphoma, non-
		. 1	by reference in its entirety. T	Hodgkins lymphoma,
			cells that may be used	Hodgkin"s disease),
			according to these assays are	melanoma, and prostate,
			publicly available (e.g.,	breast, lung, colon, pancreatic,
			through the ATCC).	esophageal, stomach, brain,
			Exemplary mouse T cells that	liver and urinary cancer. Other
***			may be used according to these	preferred indications include
***************************************			assays include the CTLL cell	benign dysproliferative
			line, which is a suspension	disorders and pre-neoplastic
			culture of IL-2 dependent	conditions, such as, for
			cytotoxic T cells.	example, hyperplasia,
			•	metaplasia, and/or dysplasia.
				Preferred indications include
				anemia, pancytopenia,
-	_			leukopenia, thrombocytopenia,
				acute lymphocytic anemia

Su ne Se in Al as in	the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), to test SRE Highly preferred indications include autoimmune diseases
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1324
	HNGJT54
	376

(e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described	below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and	inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly	preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below	under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example,	leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic,
the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in	Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the	content of each of which are herein incorporated by reference in its entirety. T cells that may be used	according to these assays are publicly available (e.g., through the ATCC).  Exemplary mouse T cells that may be used according to these	assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity	

	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	benign dysproliferative
	disorders and pre-neoplastic
	conditions, such as, for
	example, hyperplasia,
	metaplasia, and/or dysplasia.
	Preferred indications include
	anemia, pancytopenia,
	leukopenia, thrombocytopenia,
	Hodgkin's disease, acute
	lymphocytic anemia (ALL),
	plasmacytomas, multiple
	myeloma, Burkitt's lymphoma,
	arthritis, AIDS, granulomatous
	disease, inflammatory bowel
	disease, neutropenia,
	neutrophilia, psoriasis,
	suppression of immune
	reactions to transplanted
	organs and tissues,
	hemophilia, hypercoagulation,
	diabetes mellitus, endocarditis,
	meningitis, Lyme Disease,
	cardiac reperfusion injury, and
	asthma and allergy. An
	additional preferred indication
	is infection (e.g., an infectious
	disease as described below
	under "Infectious Disease").

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A highly preferred embodiment of the invention includes a method for	stimulating (e.g., increasing)	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., reducing) MCP-1 production. A highly	1S	infection (e.g., an infectious	disease as described below	under "Infectious Disease").	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Preferred indications include	blood disorders (e.g., as	described below under	with "Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as
MCP-1 FMAT. Assays for immunomodulatory proteins	that are produced by a large variety of cells and act to induce observing and	activation of monocytes and T	cells are well known in the art	and may be used or routinely	modified to assess the ability of nolynentides of the	invention (including antibodies	and agonists or antagonists of	the invention) to mediate	immunomodulation, induce	chemotaxis, and modulate	immune cell activation.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of cell	surface markers, such as	monocyte chemoattractant	protein (MCP), and the	activation of monocytes and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays
Production of MCP-1																										
1324																										·
HNGJT54	···																									
376									-											-						_

disclosed in Miraglia et al., J	described below). Preferred
<u>~</u>	clu
	anemia, pancytopenia,
"Lymphocytes: a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	lymphocytic anemia (ALL),
Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
158:2919-2925 (1997), the	disease, inflammatory bowel
contents of each of which are	disease, sepsis, neutropenia,
herein incorporated by	neutrophilia, psoriasis,
reference in its entirety.	suppression of immune
Human dendritic cells that may	reactions to transplanted
be used according to these	organs and tissues,
assays may be isolated using	hemophilia, hypercoagulation,
techniques disclosed herein or	diabetes mellitus, endocarditis,
otherwise known in the art.	meningitis (bacterial and
Human dendritic cells are	viral), Lyme Disease, asthma,
antigen presenting cells in	and allergy Preferred
suspension culture, which,	indications also include
when activated by antigen	neoplastic diseases (e.g.,
and/or cytokines, initiate and	leukemia, lymphoma, and/or as
upregulate T cell proliferation	described below under
and functional activities.	"Hyperproliferative
	Disorders"). Highly preferred
	indications include neoplasms
	and cancers, such as, leukemia,
	lymphoma, prostate, breast,
	lung, colon, pancreatic,
	esophageal, stomach, brain,

					liver, and urinary cancer. Other preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	HNGKN89	1325	Activation of	Assays for the activation of	A highly preferred indication
377			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
			•	polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
				functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
				may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
			,	signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic

transcription factor CREB (CRE binding protein).
Exemplary assays for transcription through the
cAMP response element that
may be used or routinely
modified to test cAMP-
response element activity of
polypeptides of the invention
(including antibodies and
agonists or antagonists of the
invention) include assays
disclosed in Berger et al., Gene
66:1-10 (1998); Cullen and
Malm, Methods in Enzymol
216:362-368 (1992); Henthorn
et al., Proc Natl Acad Sci USA
85:6342-6346 (1988); Reusch
et al., Mol Cell Biol
20(3):1008-1020 (2000); and
Klemm et al., J Biol Chem
273:917-923 (1998), the
contents of each of which are
herein incorporated by
reference in its entirety. Pre-
adipocytes that may be used
according to these assays are
publicly available (e.g.,
through the ATCC) and/or
may be routinely generated.
Exemplary mouse adipocyte

		Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include
cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.		This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or
	SEAP in HIB/CRE	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).
	1325	1325
	HNGKN89	HNGKN89
	377	377

rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia,	lymphoma, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and	urinary tract cancers and/or as described below under "Hyperproliferative Disorders"). Other preferred	indications include benign dysproliferative disorders and pre-neoplastic conditions, such as. for example, hyperplasia.	metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,	granulomatous disease, inflammatory bowel disease,
regulate GATA3 transcription factors and modulate expression of mast cell genes important for immune response	development. Exemplary assays for transcription through the GATA3 response element that may be used or	routinely modified to test GATA3-response element activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85-6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp Quant Biol 64:563-571 (1999); Rodriguez-Palmero et al., Eur J Immunol 29(12):3914-3924	(1999); Zheng and Flavell, Cell 89(4):587-596 (1997); and Henderson et al., Mol Cell Biol 14(6):4286-4294 (1994), the contents of each of which are	herein incorporated by reference in its entirety. Mast
							,

				cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
377	HNGKN89	1325	Activation of transcription through NFAT response element in immune cells (such as mast cells).	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include

 	agonists or antagonists of the		
•	invention) to regulate NFAT	lupus erythematosis, multiple	
 -	transcription factors and	sclerosis and/or as described	
 	modulate expression of genes		
	involved in	immunodeficiencies (e.g., as	
	immunomodulatory functions.	s.   described below). Preferred	
	Exemplary assays for	indications include neoplastic	
	transcription through the	diseases (e.g., leukemia,	
	NFAT response element that	lymphoma, melanoma,	
	may be used or routinely	prostate, breast, lung, colon,	
	modified to test NFAT-	pancreatic, esophageal,	
	response element activity of	stomach, brain, liver, and	
 	polypeptides of the invention	urinary tract cancers and/or as	
 	(including antibodies and	described below under	
	agonists or antagonists of the	"Hyperproliferative	
	invention) include assays	Disorders"). Other preferred	
	disclosed in Berger et al., Gene	ne   indications include benign	
	66:1-10 (1998); Cullen and	dysproliferative disorders and	
<del></del>	Malm, Methods in Enzymol	pre-neoplastic conditions, such	
	216:362-368 (1992); Henthorn	m as, for example, hyperplasia,	
	et al., Proc Natl Acad Sci USA	A   metaplasia, and/or dysplasia.	
	85:6342-6346 (1988); De Boer	er   Preferred indications include	
	et al., Int J Biochem Cell Biol	l anemia, pancytopenia,	
	31(10):1221-1236 (1999); Ali		
	et al., J Immunol	leukemias, Hodgkin's disease,	
	165(12):7215-7223 (2000);	acute lymphocytic anemia	
	Hutchinson and McCloskey, J	J (ALL), plasmacytomas,	
	Biol Chem 270(27):16333-		
	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,	
 	al., J Exp Med 188:527-537	granulomatous disease,	
	(1998), the contents of each of	of inflammatory bowel disease,	

			which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
HNGOM56	1326	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or

	genes in many cell types.	"Cardiovascular Disorders"),
	Exemplary assays for	Highly preferred indications
	transcription through the SRE	include autoimmune diseases
	that may be used or routinely	(e.g., rheumatoid arthritis,
	modified to test SRE activity	systemic lupus erythematosis,
	of the polypeptides of the	Crohn"s disease, multiple
	invention (including antibodies	sclerosis and/or as described
	and agonists or antagonists of	below), immunodeficiencies
	the invention) include assays	(e.g., as described below),
	disclosed in Berger et al., Gene	boosting a T cell-mediated
	66:1-10 (1998); Cullen and	immune response, and
	Malm, Methods in Enzymol	suppressing a T cell-mediated
	216:362-368 (1992); Henthorn	immune response. Additional
	et al., Proc Natl Acad Sci USA	highly preferred indications
	85:6342-6346 (1988); Benson	include inflammation and
	et al., J Immunol 153(9):3862-	inflammatory disorders, and
	3873 (1994); and Black et al.,	treating joint damage in
	Virus Genes 12(2):105-117	patients with rheumatoid
	(1997), the content of each of	arthritis. An additional highly
	which are herein incorporated	preferred indication is sepsis.
	by reference in its entirety.	Highly preferred indications
	Human T cells that may be	include neoplastic diseases
	used according to these assays	(e.g., leukemia, lymphoma,
	are publicly available (e.g.,	and/or as described below
	through the ATCC).	under "Hyperproliferative
	Exemplary human T cells that	Disorders"). Additionally,
	may be used according to these	highly preferred indications
	assays include the JURKAT	include neoplasms and
	cell line, which is a suspension	cancers, such as, leukemia,
	culture of leukemia cells that	lymphoma, melanoma, glioma
	produce IL-2 when stimulated.	(e.g., malignant glioma), solid

	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	notional material individual	ממחווסוומו לוכוכוול ושווחוומו לוכוכוול ווומוסמוחוומו לוכוכוול ווומוסמוחוו
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					disease as described below under "Infectious Disease").
379	HNGOU56	1327	Protection from Endothelial Cell	Caspase Apoptosis Rescue.	A highly preferred
			Apoptosis.	rescue are well known in the	includes a method for
			•	art and may be used or	stimulating endothelial cell
				routinely modified to assess	growth. An alternative highly
				the ability of the polypeptides	preferred embodiment of the
				of the invention (including	invention includes a method
				antibodies and agonists or	for inhibiting endothelial cell
				antagonists of the invention) to	growth. A highly preferred
				inhibit caspase protease-	embodiment of the invention
				mediated apoptosis.	includes a method for
				Exemplary assays for caspase	stimulating endothelial cell
				apoptosis that may be used or	proliferation. An alternative
				routinely modified to test	highly preferred embodiment
				caspase apoptosis rescue of	of the invention includes a
				polypeptides of the invention	method for inhibiting
				(including antibodies and	endothelial cell proliferation.
				agonists or antagonists of the	A highly preferred
				invention) include the assays	embodiment of the invention
				disclosed in Romeo et al.,	includes a method for
,				Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
				(2000); Messmer et al., Br J	growth. An alternative highly
				Pharmacol 127(7): 1633-1640	preferred embodiment of the
				(1999); and J Atheroscler	invention includes a method
				Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
				the contents of each of which	growth. A highly preferred
				are herein incorporated by	embodiment of the invention
				reference in its entirety.	includes a method for
				Endothelial cells that may be	stimulating apoptosis of

	used accord	used according to these assays	endothelial cells An
	are publicly	are publicly available (e.g.,	alternative highly preferred
	through con	through commercial sources).	embodiment of the invention
	Exemplary	Exemplary endothelial cells	includes a method for
	that may be	that may be used according to	inhibiting (e.g., decreasing)
	these assays	these assays include bovine	apoptosis of endothelial cells.
	aortic endothelial cells	thelial cells	A highly preferred
	(bAEC), wh	(bAEC), which are an example	embodiment of the invention
	of endotheli	of endothelial cells which line	includes a method for
	blood vesse	blood vessels and are involved	stimulating angiogenisis. An
	in functions	in functions that include, but	alternative highly preferred
	are not limited to,	ted to,	embodiment of the invention
	angiogenesis, vascular	is, vascular	includes a method for
	permeability	permeability, vascular tone,	inhibiting angiogenesis. A
	and immune	and immune cell extravasation.	highly preferred embodiment
-			of the invention includes a
			method for reducing cardiac
			hypertrophy. An alternative
			highly preferred embodiment
			of the invention includes a
			method for inducing cardiac
			hypertrophy. Highly
			preferred indications include
			neoplastic diseases (e.g., as
			described below under
			"Hyperproliferative
			Disorders"), and disorders of
			the cardiovascular system
			(e.g., heart disease, congestive
			heart failure, hypertension,
			aortic stenosis,

cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	
												<b>3-1</b>																		

sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s
											-						,													

	phenomenom. aneurvsms.
	restenosis: venous and
	Ivmphatic disorders such as
	thrombophlebitis,
	lymphangitis, and
	lymphedema; and other
	vascular disorders such as
	peripheral vascular disease,
	and cancer. Highly
	preferred indications also
	include trauma such as
	wounds, burns, and injured
	tissue (e.g., vascular injury
	such as, injury resulting from
	balloon angioplasty, and
	atheroschlerotic lesions),
	implant fixation, scarring,
	ischemia reperfusion injury,
	rheumatoid arthritis,
	cerebrovascular disease, renal
	diseases such as acute renal
	failure, and osteoporosis.
	Additional highly preferred
	indications include stroke,
	graft rejection, diabetic or
	other retinopathies, thrombotic
	and coagulative disorders,
	vascularitis, lymph
	angiogenesis, sexual disorders,
	age-related macular
	degeneration, and treatment

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Thromb 3(2): 75-80 (1996):	for inhibiting endothelial cell
 the contents of each of which	growth. A highly preferred
are herein incorporated by	ent
reference in its entirety.	includes a method for
Endothelial cells that may be	stimulating apoptosis of
used according to these assays	endothelial cells. An
are publicly available (e.g.,	alternative highly preferred
through commercial sources).	embodiment of the invention
Exemplary endothelial cells	includes a method for
that may be used according to	inhibiting (e.g., decreasing)
these assays include bovine	apoptosis of endothelial cells.
aortic endothelial cells	A highly preferred
(bAEC), which are an example	
of endothelial cells which line	includes a method for
blood vessels and are involved	stimulating angiogenisis. An
in functions that include, but	alternative highly preferred
are not limited to,	embodiment of the invention
angiogenesis, vascular	includes a method for
permeability, vascular tone,	inhibiting angiogenesis. A
and immune cell extravasation.	highly preferred embodiment
	of the invention includes a
	method for reducing cardiac
	hypertrophy. An alternative
	highly preferred embodiment
	of the invention includes a
	method for inducing cardiac
	hypertrophy. Highly
	preferred indications include
	neoplastic diseases (e.g., as
	described below under
	"Hyperproliferative

cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors,	leukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary	angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease,

such as, atherosclerosis, hypertension, coronary artery	disease, inflammatory	disease and Reynaud's	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic
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																			_									

and coagulative disorders,	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,
																		-											
											-			-															
													•••		-									•					

					inflammatory bowel disease
					and Crohn's disease), and pain management.
380	HNGOW62	1328	IL-10 in Human T- cell 293T		0
380	HNGOW62	1328	TNFa in Human T-cell 293T		
381	HNHAH01	1329	Activation or inhibition of	This reporter assay measures activation or inhibition of the	
			transcription through NFKB	NFkB signaling pathway in Ku812 human basophil cell	
			response element in	line. Assays for the activation	
			immune cells (such	or inhibition of transcription	
			as basophils).	through the NFKB response	
			8.844	element are well-known in the	
				art and may be used or	
				routinely modified to assess	
				the ability of polypeptides of	
				the invention (including	
			-	antibodies and agonists or	
				antagonists of the invention) to	
				regulate NFKB transcription	
				factors and modulate	
				expression of	
				immunomodulatory genes.	
				NFkB is important in the	
				pathogenesis of asthma.	
				Exemplary assays for	
				transcription through the	
				NFKB response element that	
				may be used or rountinely	

modified to test NFKB-	response element activity of	polypeptides of the invention	including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Cells were pretreated with SID	supernatants or controls for 15-	18 hours, and then 10 ng/mL	of TNF was added to stimulate	the NFkB reporter. SEAP	activity was measured after 48	hours. Basophils that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary human basophil	cell lines that may be used	according to these assays	include Ku812, originally
																								- ALC -						

1329
J

				incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be	
	HNHCX60	1330	Activation of	include microvascular endothelial cells (MVEC).  Assays for the activation of	A highly preferred indication
382			transcription through cAMP response element (CRE) in pre-	transcription through the cAMP response element are well-known in the art and may be used or routinely modified	is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss
			adipocytes.	to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP,	or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication
				regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. For example, a	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other
				313-L1/CRE reporter assay may be used to identify factors that activate the cAMP signaling pathway. CREB plays a major role in adipogenesis, and is involved	diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic

		in differentiation into	neuropathy), blood vessel
		adipocytes. CRE contains the	blockage, heart disease, stroke,
		binding sequence for the	impotence (e.g., due to diabetic
		transcription factor CREB	neuropathy or blood vessel
		(CRE binding protein).	blockage), seizures, mental
		Exemplary assays for	confusion, drowsiness,
		transcription through the	nonketotic hyperglycemic-
		cAMP response element that	hyperosmolar coma,
		may be used or routinely	cardiovascular disease (e.g.,
		modified to test cAMP-	heart disease, atherosclerosis,
-		response element activity of	microvascular disease,
		polypeptides of the invention	hypertension, stroke, and other
		(including antibodies and	diseases and disorders as
	-	agonists or antagonists of the	described in the
		invention) include assays	"Cardiovascular Disorders"
		disclosed in Berger et al., Gene	section below), dyslipidemia,
		66:1-10 (1998); Cullen and	endocrine disorders (as
		Malm, Methods in Enzymol	described in the "Endocrine
		216:362-368 (1992); Henthorn	Disorders" section below),
		et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
		85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
		et al., Mol Cell Biol	blindness), ulcers and impaired
		20(3):1008-1020 (2000); and	wound healing, and infection
		Klemm et al., J Biol Chem	(e.g., infectious diseases and
		273:917-923 (1998), the	disorders as described in the
		contents of each of which are	"Infectious Diseases" section
		herein incorporated by	below, especially of the
		reference in its entirety. Pre-	urinary tract and skin), carpal
		adipocytes that may be used	tunnel syndrome and
		according to these assays are	Dupuytren's contracture).
		publicly available (e.g.,	Additional highly preferred

indications are complications associated with insulin resistance.	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic
through the ATCC) and/or may be routinely generated. Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of
	Activation of transcription through AP1 response element in immune cells (such as T-cells).
	1330
	HNHCX60
	382

		polypeptides of the invention (including antibodies and	lupus erythematosis, multiple sclerosis and/or as described
		agonists or antagonists of the	below) and
		invention) include assays	immunodeficiencies (e.g., as
		disclosed in Berger et al., Gene	described below). Additional
		66:1-10 (1988); Cullen and	highly preferred indications
		Malm, Methods in Enzymol	include inflammation and
		216:362-368 (1992); Henthorn	inflammatory disorders.
		et al., Proc Natl Acad Sci USA	Highly preferred indications
		85:6342-6346 (1988);	also include neoplastic
		Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
		272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
		18(9):4986-4993 (1998); and	"Hyperproliferative
-		Fraser et al., Eur J Immunol	Disorders"). Highly preferred
		29(3):838-844 (1999), the	indications include neoplasms
		contents of each of which are	and cancers, such as, leukemia,
		herein incorporated by	lymphoma, prostate, breast,
		reference in its entirety. T	lung, colon, pancreatic,
		cells that may be used	esophageal, stomach, brain,
		according to these assays are	liver, and urinary cancer. Other
		publicly available (e.g.,	preferred indications include
		through the ATCC).	benign dysproliferative
		Exemplary mouse T cells that	disorders and pre-neoplastic
		may be used according to these	conditions, such as, for
		assays include the CTLL cell	example, hyperplasia,
	-	line, which is an IL-2	metaplasia, and/or dysplasia.
		dependent suspension-culture	Preferred indications include
		cell line with cytotoxic	arthritis, asthma, AIDS,
		activity.	allergy, anemia, pancytopenia,
			leukopenia, thrombocytopenia,

Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus
	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention
	Production of IFNgamma using a T cells
	1331
	HNHCY64
	383

	(including antibodies and	osteoporosis, and/or as
	agonists or antagonists of the	described below under
	invention) to mediate	"Infectious Disease"). Highly
	immunomodulation, regulate	preferred indications include
	inflammatory activities,	autoimmune disease (e.g.,
	modulate TH2 helper cell	rheumatoid arthritis, systemic
	function, and/or mediate	lupus erythematosis, multiple
	humoral or cell-mediated	sclerosis and/or as described
	immunity. Exemplary assays	below), immunodeficiency
	that test for	(e.g., as described below),
	immunomodulatory proteins	boosting a T cell-mediated
	evaluate the production of	immune response, and
	cytokines, such as Interferon	suppressing a T cell-mediated
ng company	gamma (IFNg), and the	immune response. Additional
MA ALA	activation of T cells. Such	highly preferred indications
	assays that may be used or	include inflammation and
	routinely modified to test	inflammatory disorders.
	immunomodulatory activity of	Additional preferred
	polypeptides of the invention	indications include idiopathic
	(including antibodies and	pulmonary fibrosis. Highly
	agonists or antagonists of the	preferred indications include
	invention) include the assays	neoplastic diseases (e.g.,
	disclosed in Miraglia et al., J	leukemia, lymphoma,
	Biomolecular Screening 4:193-	melanoma, and/or as described
	204 (1999); Rowland et al.,	below under
	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); Gonzalez et al., J Clin	indications include neoplasms
a	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
 	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,

				et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
				15:749-795 (1997), and	esophageal, stomach, brain,
				Rheumatology (Oxford)	liver and urinary cancer. Other
				38(3):214-20 (1999), the	preferred indications include
				contents of each of which are	benign dysproliferative
				herein incorporated by	disorders and pre-neoplastic
				reference in its entirety.	conditions, such as, for
				Human T cells that may be	example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
				techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
				human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
				CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
				be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HNHCY94	1332	Activation of	Assays for the activation of	Preferred indications
384			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are known in	(e.g., as described below under
			response element in	the art and may be used or	"Hyperproliferative

immune cells (such	routinely modified to assess	Disorders"), blood disorders
as T-cells).	the ability of polypeptides of	(e.g., as described below under
	the invention (including	"Immune Activity",
	antibodies and agonists or	"Cardiovascular Disorders",
 	antagonists of the invention) to	and/or "Blood-Related
	modulate growth and other cell	Disorders"), and infection
	functions. Exemplary assays	(e.g., an infectious disease as
	for transcription through the	described below under
	AP1 response element that	"Infectious Disease"). Highly
	may be used or routinely	preferred indications include
	modified to test AP1-response	autoimmune diseases (e.g.,
 	element activity of	rheumatoid arthritis, systemic
	polypeptides of the invention	lupus erythematosis, multiple
	(including antibodies and	sclerosis and/or as described
	agonists or antagonists of the	below) and
	invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety. T	lung, colon, pancreatic,

			cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatory bowel disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis,
HNHDW38	1333	CD71 in Human T cells		members, and raying Discuss.
HNHDW42	1334	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment

	role in mucosal immunity).	al immunity).	of the invention includes a
	IL-6 induces c	IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
	Deregulated ex	Deregulated expression of IL-6	reducing) IL-6 production. A
	has been linke	has been linked to autoimmune	highly preferrred indication is
	disease, plasmacytomas,	lacytomas,	the stimulation or enhancement
	myelomas, and chronic	d chronic	of mucosal immunity. Highly
	hyperproliferative diseases.	tive diseases.	preferred indications include
	Assays for imr	Assays for immunomodulatory	blood disorders (e.g., as
	and differentiation factor	tion factor	described below under
	proteins produced by a large	ced by a large	"Immune Activity", "Blood-
	variety of cells where the	s where the	Related Disorders", and/or
	expression level is strongly	el is strongly	"Cardiovascular Disorders"),
	regulated by cy	regulated by cytokines, growth	and infection (e.g., as
	factors, and ho	factors, and hormones are well	described below under
	known in the a	known in the art and may be	"Infectious Disease"). Highly
	used or routine	used or routinely modified to	preferred indications include
	assess the ability of	ity of	autoimmune diseases (e.g.,
	polypeptides o	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lbodies and	lupus erythematosis, multiple
-	agonists or ant	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	nediate	below) and
	immunomodulation and	lation and	immunodeficiencies (e.g., as
	differentiation	differentiation and modulate T	described below). Highly
	cell proliferation	cell proliferation and function.	preferred indications also
	Exemplary ass	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	latory proteins	mediated immune response
	evaluate the production of	oduction of	and alternatively suppressing a
	cytokines, such as IL-6, and	h as IL-6, and	B cell-mediated immune
-	the stimulation and	l and	response. Highly preferred
	upregulation of T cell	f T cell	indications include
	proliferation and functional	nd functional	inflammation and

	may be used or routinely modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention	disorders.Additional highly	
	modified to test immunomodulatory and diffferentiation activity of polypeptides of the invention	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	
	immunomodulatory and diffferentiation activity of polypeptides of the invention	preferred indications include	
	diffferentiation activity of polypeptides of the invention	asthma and allergy. Highly	
	polypeptides of the invention	preferred indications include	
		neoplastic diseases (e.g.,	
	(including antibodies and	myeloma, plasmacytoma,	
	agonists or antagonists of the	leukemia, lymphoma,	
	invention) include assays	melanoma, and/or as described	
	disclosed in Miraglia et al., J	below under	
_	Biomolecular Screening 4:193-	"Hyperproliferative	
	204(1999); Rowland et al.,	Disorders"). Highly preferred	
	"Lymphocytes: a practical	indications include neoplasms	
	approach" Chapter 6:138-160	and cancers, such as, myeloma,	
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,	
	Immunol 158:2919-2925	lymphoma, melanoma, and	
	(1997), the contents of each of	prostate, breast, lung, colon,	
	which are herein incorporated	pancreatic, esophageal,	
	by reference in its entirety.	stomach, brain, liver and	
	Human dendritic cells that may	urinary cancer. Other preferred	
	be used according to these	indications include benign	
	assays may be isolated using	dysproliferative disorders and	
	techniques disclosed herein or	pre-neoplastic conditions, such	
	otherwise known in the art.	as, for example, hyperplasia,	
	Human dendritic cells are	metaplasia, and/or dysplasia.	
	antigen presenting cells in	Preferred indications include	
	suspension culture, which,	anemia, pancytopenia,	
	when activated by antigen	leukopenia, thrombocytopenia,	
	and/or cytokines, initiate and	Hodgkin's disease, acute	
	upregulate T cell proliferation	lymphocytic anemia (ALL),	
	and functional activities.	multiple myeloma, Burkitt's	-

lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	CD69 in Human T cells	Hexosaminidase in RBL-2H3	Production of IL-6 FMAT. IL-6 is produced by T cells and has strong embodiment of the invention effects on B cells. IL-6 participates in IL-4 induced lgE production and increases IgA production (IgA plays a role in mucosal immunity).  IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune highly preferrred indication is
	1334	1334	1335
	HNHDW42	HNHDW42	HNHED17
	386	386	387

	myelon	myelomas, and chronic	of mucosal imminity. Highly
	hyperpi	hyperproliferative diseases.	preferred indications include
	Assays	Assays for immunomodulatory	blood disorders (e.g., as
	and diff	and differentiation factor	described below under
	proteins	proteins produced by a large	"Immune Activity", "Blood-
	variety	variety of cells where the	Related Disorders", and/or
	express	expression level is strongly	"Cardiovascular Disorders"),
	regulate	regulated by cytokines, growth	and infection (e.g., as
	factors,	factors, and hormones are well	described below under
	known	known in the art and may be	"Infectious Disease"). Highly
	used or	used or routinely modified to	preferred indications include
	assess t	assess the ability of	autoimmune diseases (e.g.,
	polypep	polypeptides of the invention	rheumatoid arthritis, systemic
	includi (includi	(including antibodies and	lupus erythematosis, multiple
	agonists	agonists or antagonists of the	sclerosis and/or as described
	inventic	invention) to mediate	below) and
	immunc	immunomodulation and	immunodeficiencies (e.g., as
	differen	differentiation and modulate T	described below). Highly
-	cell pro	cell proliferation and function.	preferred indications also
	Exempl	Exemplary assays that test for	include boosting a B cell-
	immunc	immunomodulatory proteins	mediated immune response
	evaluate	evaluate the production of	and alternatively suppressing a
	cytokine cytokine	cytokines, such as IL-6, and	B cell-mediated immune
	the stim	the stimulation and	response. Highly preferred
	upregul	upregulation of T cell	indications include
	prolifera	proliferation and functional	inflammation and
	activitie	activities. Such assays that	inflammatory
	may be	may be used or routinely	disorders. Additional highly
	modifie	modified to test	preferred indications include
	immuno	immunomodulatory and	asthma and allergy. Highly
	diffferen	diffferentiation activity of	preferred indications include

	polypeptides of the invention	neoplastic diseases (e.g
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
•	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.
	antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,
	when activated by antigen	leukopenia, thrombocytopenia,
	and/or cytokines, initiate and	Hodgkin's disease, acute
	upregulate T cell proliferation	lymphocytic anemia (ALL),
	and functional activities.	multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,
		granulomatous disease,
		inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,

suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	36 SEAP in HIB/CRE	Production of GM-  CSF  CSF  CSF  CSF  CSF  CSF  CSF  CS
	1336 SE	1336 Pro CS
	HNHEI42	HNHE142
	388	388

	proteins that promote the	neutropenia (and the
	production of GM-CSF are	prevention of neutropenia
 	well known in the art and may	(e.g., in HIV infected patients),
 	be used or routinely modified	and/or as described below
	to assess the ability of	under "Immune Activity",
	polypeptides of the invention	"Blood-Related Disorders",
	(including antibodies and	and/or "Cardiovascular
 	agonists or antagonists of the	Disorders"). Highly preferred
	invention) to mediate	indications also include
,	immunomodulation and	autoimmune diseases (e.g.,
	modulate the growth and	rheumatoid arthritis, systemic
- 100	differentiation of leukocytes.	lupus erythematosis, multiple
	Exemplary assays that test for	sclerosis and/or as described
	immunomodulatory proteins	below) and
	evaluate the production of	immunodeficiencies (e.g., as
 	cytokines, such as GM-CSF,	described below). Additional
 	and the activation of T cells.	highly preferred indications
	Such assays that may be used	include asthma. Highly
 	or routinely modified to test	preferred indications include
 	immunomodulatory activity of	neoplastic diseases (e.g.,
77-	polypeptides of the invention	leukemia (e.g., acute
 	(including antibodies and	lymphoblastic leukemia, and
	agonists or antagonists of the	acute myelogenous leukemia),
	invention) include the assays	lymphoma (e.g., non-
	disclosed in Miraglia et al., J	Hodgkin"s lymphoma and
	Biomolecular Screening 4:193-	Hodgkin"s disease), and/or as
-	204 (1999); Rowland et al.,	described below under
	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); and Ye et al., J Leukoc	indications include neoplasms
	Biol (58(2):225-233, the	and cancers, such as, leukemia,

contents of each of which are herein incorporated by reference in its entirety.  Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC) or may be isolated using techniques disclosed herein or otherwise known in the art. Natural killer (NK) cells are large granular lymphocytes that have cytotoxic activity but do bind antigen. NK cells show antibody-independent killing of tumor cells and also recognize antibody bound on target cells, via NK Fc receptors, leading to cellmediated cytotoxicity.	lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications include: suppression of immune reactions to transplanted organs and tissues (e.g., bone marrow transplant); accelerating myeloid recovery; and mobilizing hematopoietic progenitor cells. Preferred indications include boosting a T cell-mediated immune response, and alternatively, suppressing a T cell-mediated indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute
	plasmacytomas, multiple myeloma Burkitt's lymphoma
	arthritis, AIDS, granulomatous disease, inflammatory bowel

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"Thmune Activity", and "Blood-Related Disorders"). Preferred indications include autoimmune diseases (e.g.,	lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below).					
immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely	modified to test NFKB- response element activity of polypeptides of the invention	(including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997);	Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated	by reference in its entirety. For example, a reporter assay (which measures increases in	NFkB responsive element in EOL-1 cells) may link the NFKB element to a repeorter

		A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific
gene and binds to the NFKB transcription factor, which is upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important in the allergic responses; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Eol-1 is a human eosinophil cell line.		Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for P13 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose
	SEAP in HIB/CRE	Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway
	1338	1338
	HNHFR04	HNHFR04
	390	390

	metabolism and cell survival	embodiment skeletal muscle
-	Evemplary assays for DI3	cell proliferation is stimulated
	L'ACHIPHALY ASSAYS TOLL I	A 1,
	Kinase activity that may be	An alternative highly preferred
	used or routinely modified to	embodiment of the invention
	test PI3 kinase-induced activity	y includes a method for
	of polypeptides of the	inhibiting muscle cell
	invention (including antibodies	s proliferation. In a specific
	and agonists or antagonists of	
	the invention) include assays	cell proliferation is inhibited.
	disclosed in Forrer et al., Biol	A preferred embodiment of
	Chem 379(8-9):1101-1110	the invention includes a
	(1998); Nikoulina et al.,	method for stimulating muscle
	Diabetes 49(2):263-271	cell differentiation. In a
	(2000); and Schreyer et al.,	specific embodiment, skeletal
	Diabetes 48(8):1662-1666	muscle cell differentiation is
	(1999), the contents of each of	stimulated. An alternative
	which are herein incorporated	highly preferred embodiment
	by reference in its entirety.	of the invention includes a
	Rat myoblast cells that may be	method for inhibiting muscle
-	used according to these assays	cell differentiation. In a
	are publicly available (e.g.,	specific embodiment, skeletal
	through the ATCC).	muscle cell differentiation is
-	Exemplary rat myoblast cells	inhibited. Highly preferred
	that may be used according to	indications include disorders of
	these assays include L6 cells.	the musculoskeletal system.
	L6 is an adherent rat myoblast	
	cell line, isolated from primary	neoplastic diseases (e.g., as
	cultures of rat thigh muscle,	described below under
	that fuses to form	"Hyperproliferative
	multinucleated myotubes and	Disorders"), endocrine
	striated fibers after culture in	disorders (e.g., as described

below under "Endocrine	Disorders"), neural disorders	(e.g., as described below under	"Neural Activity and	Neurological Diseases"), blood	disorders (e.g., as described	below under "Immune	Activity", "Cardiovascular	Disorders", and/or "Blood-	Related Disorders"), immune	disorders (e.g., as described	below under "Immune	Activity"), and infection (e.g.,	as described below under	"Infectious Disease"). A	highly preferred indication is	diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.,	due to diabetic neuropathy),	blood vessel blockage, heart
differentiation media.																														
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	tunnel syndrome and	Dupuytren's contracture).  An additional highly preferred indication is obesity and/or

complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additonal highly preferred	indications are disorders of the	musculoskeletal system	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include: myopathy,	atrophy, congestive heart	failure, cachexia, myxomas,	fibromas, congenital	cardiovascular abnormalities,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Highly	preferred indications include	neoplasms and cancer, such as,	rhabdomyoma,	rhabdosarcoma, stomach,	esophageal, prostate, and	urinary cancer. Preferred	indications also include breast,	lung, colon, pancreatic, brain,
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					and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.
390	HNHFR04	1338	Activation of transcription through NFKB response element in neuronal cells (such as SKNMC cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis,
				polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of neuronal genes. Exemplary assays for transcription	prevention, and/or treatment of Neurological Diseases and Disorders (e.g. Alzheimer"s Disease, Parkinson's Disease, Brain Cancer, Seizures).
				through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gill JS, et al., Neurobiol Dis, 7(4):448-461	

	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),
(2000); Tamatani M, et al., J Biol Chem, 274(13):8531-8538 (1999); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Neuronal cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary neuronal cells that may be used according to these assays include the SKNMC neuronal cell line.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of
	Activation of transcription through cAMP response element in immune cells (such as T-cells).
	1339
	HNHFU32
	391

Infectious Preferred clude liseases (e.g.,	referred lude iseases (e.g.,	lude iseases (e.g.,	iseases (e.g.,		rheumatoid arthritis, systemic	lupus erythematosis, multiple	r as described	nodeficiencies	bed below),	ell-mediated	nse, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	put	disorders.	ed indications	stic diseases	, lymphoma,	ribed below	roliferative	Disorders"). Highly preferred	indications include neoplasms	ich as, for	example, leukemia, lymphoma	nphoma,	homa, non-	phoma,	ease),
infectious disease as described	; ;	Disease").	indications include	autoimmune diseases (e.g.,	rheumatoid art	lupus erythema	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a	immune respoi	preferred indic	inflammation and	inflammatory disorders.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). H	indications inc	and cancers, such as, for	example, leuke	(e.g., T cell lymphoma,	Burkitt's lymphoma, non-	Hodgkins lymphoma,	Hodgkin's disease),
polypeptides of the invention (including antibodies and	agonists or antagonists of the	invention) to increase cAMP	and regulate CREB	transcription factors, and	modulate expression of genes	involved in a wide variety of	cell functions. Exemplary	assays for transcription	through the cAMP response	element that may be used or	routinely modified to test	cAMP-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Genes 15(2):105-117	(1997); and Belkowski et al., J	Immunol 161(2):659-665	(1998), the contents of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used
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				according to these assays are	melanoma, and prostate,
				publicly available (e.g.,	breast, lung, colon, pancreatic,
				through the ATCC).	esophageal, stomach, brain,
				Exemplary mouse T cells that	liver and urinary cancer. Other
				may be used according to these	preferred indications include
				assays include the CTLL cell	benign dysproliferative
				line, which is a suspension	disorders and pre-neoplastic
				culture of IL-2 dependent	conditions, such as, for
				cytotoxic T cells.	example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
391	HNHFU32	1339	SEAP in HIB/CRE	,	
392	HNHOD46	1340	SEAP in 293/ISRE		
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A highly preferred embodiment of the invention	includes a method for	stimulating adipocyte	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	adipocyte proliferation. A	highly preferred embodiment	of the invention includes a	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation. A highly	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under
Kinase assay. Kinase assays, for example an Elk-1 kinase	assay, for ERK signal	transduction that regulate cell	proliferation or differentiation	are well known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature
Activation of Adipocyte ERK	Signaling Pathway																	<del></del>											
1340	-							7847																					
HNHOD46																													
392								_																					

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"Endocrine Disorders"). Highly preferred indications	diseases (e.g., lipomas,	iiposarcomas, and/or as described below under			indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,
410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999):	the contents of each of which	are nerein incorporated by reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.								
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diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	
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blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section	urinary tract and skin). An additional highly preferred indication is obesity and/or complications associated with	preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	indications are disorders of the musculoskeletal systems including myopathies, described herein.	Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or
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		promoter) and to regulate	diabetic neuropathy, nerve
		insulin production. The	disease and nerve damage
		DMEF1 response element is	(e.g., due to diabetic
		present in the GLUT4	neuropathy), blood vessel
•		promoter and binds to MEF2	blockage, heart disease, stroke,
		transcription factor and another	impotence (e.g., due to diabetic
		transcription factor that is	neuropathy or blood vessel
		required for insulin regulation	blockage), seizures, mental
		of Glut4 expression in skeletal	confusion, drowsiness,
		muscle. GLUT4 is the primary	nonketotic hyperglycemic-
		insulin-responsive glucose	hyperosmolar coma,
		transporter in fat and muscle	cardiovascular disease (e.g.,
		tissue. Exemplary assays that	heart disease, atherosclerosis,
		may be used or routinely	microvascular disease,
	-	modified to test for DMEF1	hypertension, stroke, and other
		response element activity (in	diseases and disorders as
		adipocytes and pre-adipocytes)	described in the
		by polypeptides of the	"Cardiovascular Disorders"
		invention (including antibodies	section below), dyslipidemia,
		and agonists or antagonists of	endocrine disorders (as
		the invention) include assays	described in the "Endocrine
		disclosed in Thai, M.V., et al., J	Disorders" section below),
		Biol Chem, 273(23):14285-92	neuropathy, vision impairment
		(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
		Chem, 275(21):16323-8	blindness), ulcers and impaired
		(2000); Liu, M.L., et al., J Biol	wound healing, and infection
		Chem, 269(45):28514-21	(e.g., infectious diseases and
		(1994); "Identification of a 30-	disorders as described in the
		base pair regulatory element	"Infectious Diseases" section
		and novel DNA binding	below, especially of the
		protein that regulates the	urinary tract and skin). An

through cAMP	cAMP response element are	associated with obesity.
response element	well-known in the art and may	Additional highly preferred
(CRE) in pre-	be used or routinely modified	indications include weight loss
 adipocytes.	to assess the ability of	or alternatively, weight gain.
	polypeptides of the invention	An additional highly preferred
	(including antibodies and	indication is diabetes mellitus.
	agonists or antagonists of the	An additional highly preferred
	invention) to increase cAMP,	indication is a complication
	regulate CREB transcription	associated with diabetes (e.g.,
	factors, and modulate	diabetic retinopathy, diabetic
	expression of genes involved	nephropathy, kidney disease
	in a wide variety of cell	(e.g., renal failure,
	functions. For example, a	nephropathy and/or other
	3T3-L1/CRE reporter assay	diseases and disorders as
	may be used to identify factors	described in the "Renal
	that activate the cAMP	Disorders" section below),
	signaling pathway. CREB	diabetic neuropathy, nerve
	plays a major role in	disease and nerve damage
	adipogenesis, and is involved	(e.g., due to diabetic
	in differentiation into	neuropathy), blood vessel
	adipocytes. CRE contains the	blockage, heart disease, stroke,
	binding sequence for the	impotence (e.g., due to diabetic
	transcription factor CREB	neuropathy or blood vessel
	(CRE binding protein).	blockage), seizures, mental
	Exemplary assays for	confusion, drowsiness,
	transcription through the	nonketotic hyperglycemic-
	cAMP response element that	hyperosmolar coma,
	may be used or routinely	cardiovascular disease (e.g.,
	modified to test cAMP-	heart disease, atherosclerosis,
	response element activity of	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other

(including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
disclosed in Berger et al., Gene	section below), dyslipidemia,
66:1-10 (1998); Cullen and	endocrine disorders (as
Malm, Methods in Enzymol	described in the "Endocrine
216:362-368 (1992); Henthorn	Disorders" section below),
et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
et al., Mol Cell Biol	blindness), ulcers and impaired
20(3):1008-1020 (2000); and	wound healing, and infection
Klemm et al., J Biol Chem	(e.g., infectious diseases and
273:917-923 (1998), the	disorders as described in the
contents of each of which are	"Infectious Diseases" section
herein incorporated by	below, especially of the
reference in its entirety. Pre-	urinary tract and skin), carpal
adipocytes that may be used	tunnel syndrome and
according to these assays are	Dupuytren's contracture).
publicly available (e.g.,	Additional highly preferred
through the ATCC) and/or	indications are complications
may be routinely generated.	associated with insulin
Exemplary mouse adipocyte	resistance.
cells that may be used	
according to these assays	
include 3T3-L1 cells. 3T3-L1	
is an adherent mouse	
preadipocyte cell line that is a	
continuous substrain of 3T3	
fibroblast cells developed	
through clonal isolation and	
undergo a pre-adipocyte to	:

				adipose-like conversion under	
	-			appropriate differentiation	
				conditions known in the art.	
000	HNHOD46	1340	Activation of	Assays for the activation of	A highly preferred indication
392			transcription	transcription through the	is obesity and/or complications
	-		through serum	Serum Response Element	associated with obesity.
			response element in	(SRE) are well-known in the	Additional highly preferred
			pre-adipocytes.	art and may be used or	indications include weight loss
-				routinely modified to assess	or alternatively, weight gain.
				the ability of polypeptides of	An additional highly preferred
				the invention (including	indication is diabetes mellitus.
				antibodies and agonists or	An additional highly preferred
				antagonists of the invention) to	indication is a complication
				regulate the serum response	associated with diabetes (e.g.,
				factors and modulate the	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in growth. Exemplary assays	(e.g., renal failure,
				for transcription through the	nephropathy and/or other
				SRE that may be used or	diseases and disorders as
				routinely modified to test SRE	described in the "Renal
				activity of the polypeptides of	Disorders" section below),
				the invention (including	diabetic neuropathy, nerve
- 11				antibodies and agonists or	disease and nerve damage
				antagonists of the invention)	(e.g., due to diabetic
-10				include assays disclosed in	neuropathy), blood vessel
				Berger et al., Gene 66:1-10	blockage, heart disease, stroke,
				(1998); Cullen and Malm,	impotence (e.g., due to diabetic
				Methods in Enzymol 216:362-	neuropathy or blood vessel
				368 (1992); Henthorn et al.,	blockage), seizures, mental
				Proc Natl Acad Sci USA	confusion, drowsiness,
				85:6342-6346 (1988); and	nonketotic hyperglycemic-

				Black et al., Virus Genes	hvnerosmolar coma
				12(2):105-117 (1997), the	cardiovascular disease (e.g.
				content of each of which are	heart disease, atherosclerosis,
				herein incorporated by	microvascular disease,
	-			reference in its entirety. Pre-	hypertension, stroke, and other
_				adipocytes that may be used	diseases and disorders as
				according to these assays are	described in the
				publicly available (e.g.,	"Cardiovascular Disorders"
				through the ATCC) and/or	section below), dyslipidemia,
				may be routinely generated.	endocrine disorders (as
				Exemplary mouse adipocyte	described in the "Endocrine
			****	cells that may be used	Disorders" section below),
				according to these assays	neuropathy, vision impairment
		-		include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
				is an adherent mouse	blindness), ulcers and impaired
				preadipocyte cell line that is a	wound healing, and infection
	•			continuous substrain of 3T3	(e.g., infectious diseases and
				fibroblast cells developed	disorders as described in the
				through clonal isolation and	"Infectious Diseases" section
				undergo a pre-adipocyte to	below). Additional highly
·				adipose-like conversion under	preferred indications are
				appropriate differentiation	complications associated with
				conditions known in the art.	insulin resistance.
000	HNHOD46	1340	Activation of	Assays for the activation of	Preferred indications include
292			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
<u> </u>			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described

agonists or antagonists of the	below under "Infectious
invention) to increase cAMP	Disease"). Preferred
and regulate CREB	is in
transcription factors, and	autoimmune diseases (e.g.,
modulate expression of genes	rheumatoid arthritis, systemic
involved in a wide variety of	lupus erythematosis, multiple
cell functions. Exemplary	sclerosis and/or as described
assays for transcription	below), immunodeficiencies
through the cAMP response	(e.g., as described below),
 element that may be used or	boosting a T cell-mediated
routinely modified to test	immune response, and
 cAMP-response element	suppressing a T cell-mediated
activity of polypeptides of the	immune response. Additional
invention (including antibodies	
and agonists or antagonists of	inflammation and
the invention) include assays	inflammatory disorders.
disclosed in Berger et al., Gene	e Highly preferred indications
66:1-10 (1998); Cullen and	include neoplastic diseases
Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
216:362-368 (1992); Henthorn	
et al., Proc Natl Acad Sci USA	
85:6342-6346 (1988); Black et	Disorders"). Highly preferred
al., Virus Genes 15(2):105-117	indications include neoplasms
 (1997); and Belkowski et al., J	and cancers, such as, for
Immunol 161(2):659-665	
(1998), the contents of each of	
which are herein incorporated	Burkitt's lymphoma, non-
by reference in its entirety. T	Hodgkins lymphoma,
cells that may be used	Hodgkin"s disease),
according to these assays are	melanoma, and prostate,
publicly available (e.g.,	breast, lung, colon, pancreatic,

			,	through the ATCC).  Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and
392	HNHOD46	1340	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess	asthma and allergy.  A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the

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	invention includes a method	for stimulating (e.g.,	increasing) TNF alpha	production. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	in the contraction of the contra
	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	11 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
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(e.g., leukemia, lymphoma, and/or as described below under "Hymernroliferative	Disorders"). Additionally,	highly preferred indications include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,
Exemplary mouse T cells that may be used according to these assays include the CTLL cell	line, which is an IL-2	of T cells with cytotoxic	activity.																								
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HNHOD46	1340	Production of IL-6	IL-6 FMAT. IL-6 is produced	reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
			by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, orowth	A mgnty preserved embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as

"Infectious Disease"). Highly preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple	sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Highly	preferred indications also include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms
factors, and hormones are well known in the art and may be used or routinely modified to	assess the ability of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) to mediate	immunomodulation and differentiation and modulate T	cell proliferation and function.  Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical
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	approach" Chapter 6:138-160	and cancers, such as, myeloma.
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	   Immunol 158:2919-2925	Iymphoma, melanoma, and
	 (1997), the contents of each of	prostate, breast, lung, colon,
-	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	 be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	 techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
	 Human dendritic cells are	metaplasia, and/or dysplasia.
	 antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,
	 when activated by antigen	leukopenia, thrombocytopenia,
	and/or cytokines, initiate and	Hodgkin's disease, acute
	 upregulate T cell proliferation	lymphocytic anemia (ALL),
	 and functional activities.	multiple myeloma, Burkitt's
		lymphoma, arthritis, AIDS,
_		granulomatous disease,
		inflammatory bowel disease,
		sepsis, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
		reactions to transplanted
		organs and tissues,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
		meningitis, and Lyme Disease.
		An additional preferred
		indication is infection (e.g., an

infectious disease as described below under "Infectious Disease")	A highly preferred embodiment of the invention	includes a method for	stimulating MIP1a production.  An alternative highly preferred	embodiment of the invention	includes a method for	iSi	MIP1a production. A highly	preferred indication is	infection (e.g., an infectious	disease as described below	under "Infectious Disease").	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below): Additional	highly preferred indications
	MIP-1alpha FMAT. Assays for immunomodulatory	proteins produced by activated	dendritic cells that upregulate monocyte/macrophage and T	cell chemotaxis are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation, modulate	chemotaxis, and modulate T	cell differentiation. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	chemokines, such as	macrophage inflammatory	protein 1 alpha (MIP-1a), and	the activation of	monocytes/macrophages and T	cells. Such assays that may be	used or routinely modified to	test immunomodulatory and	chemotaxis activity of
	Production of MIP1alpha																									
	1340																									
	HNHOD46																									
	392																									

include inflammation and	inflammatory disorders.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma, and allergy.	Preferred indications also	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,
polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-	29 (2000); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation
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				and functional activities.	liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
392	HNHOD46	1340	SEAP in HIB/CRE		
392	HNHOD46	1340	Activation of transcription	This reporter assay measures activation of the GATA-3	Highly preferred indications
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
_				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as

assays for transcription	described below). Preferred
through the GATA3 response	indications include neoplastic
element that may be used or	diseases (e.g., leukemia,
routinely modified to test	lymphoma, melanoma,
GATA3-response element	prostate, breast, lung, colon,
activity of polypeptides of the	pancreatic, esophageal,
invention (including antibodies	stomach, brain, liver, and
and agonists or antagonists of	urinary tract cancers and/or as
the invention) include assays	described below under
disclosed in Berger et al., Gene	"Hyperproliferative
66:1-10 (1998); Cullen and	Disorders"). Other preferred
   Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	dysproliferative disorders and
et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
Quant Biol 64:563-571 (1999);	Preferred indications include
Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
 J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
contents of each of which are	lymphoma, arthritis, AIDS,
herein incorporated by	granulomatous disease,
reference in its entirety. Mast	inflammatory bowel disease,
cells that may be used	sepsis, neutropenia,
according to these assays are	neutrophilia, psoriasis,
publicly available (e.g.,	suppression of immune
through the ATCC).	reactions to transplanted
Exemplary human mast cells	organs and tissues, hemophilia

				that may be used according to these assays include the HMC-1 cell line, which is an	hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
_		-		many characteristics of	
				immature mast cells.	
	HNHOD46	1340	Activation of	This reporter assay measures	Highly preferred indications
392			transcription	activation of the NFAT	include allergy, asthma, and
-			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
<u> </u>				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
	,			involved in	immunodeficiencies (e.g., as

			immunomodulatory functions.	described below). Preferred
			Exemplary assays for	indications include neoplastic
			transcription through the	diseases (e.g., leukemia,
			NFAT response element that	lymphoma, melanoma,
			may be used or routinely	prostate, breast, lung, colon,
			modified to test NFAT-	pancreatic, esophageal,
			response element activity of	stomach, brain, liver, and
			polypeptides of the invention	urinary tract cancers and/or as
			(including antibodies and	described below under
			agonists or antagonists of the	"Hyperproliferative
			invention) include assays	Disorders"). Other preferred
			disclosed in Berger et al., Gene	indications include benign
			66:1-10 (1998); Cullen and	dysproliferative disorders and
			Malm, Methods in Enzymol	pre-neoplastic conditions, such
			216:362-368 (1992); Henthorn	as, for example, hyperplasia,
			et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
	,		85:6342-6346 (1988); De Boer	Preferred indications include
			et al., Int J Biochem Cell Biol	anemia, pancytopenia,
-			31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
			et al., J Immunol	leukemias, Hodgkin's disease,
			165(12):7215-7223 (2000);	acute lymphocytic anemia
			Hutchinson and McCloskey, J	(ALL), plasmacytomas,
			Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
			16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
			al., J Exp Med 188:527-537	granulomatous disease,
			(1998), the contents of each of	inflammatory bowel disease,
			which are herein incorporated	sepsis, neutropenia,
			by reference in its entirety.	neutrophilia, psoriasis,
			Mast cells that may be used	suppression of immune
			according to these assays are	reactions to transplanted
			publicly available (e.g.,	organs and tissues, hemophilia,

hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	
through the ATCC).  Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1340
	HNHOD46
	392

				nragant which with all	
				presence of metabolically	
				active cells. 3T3-L1 is a	
				mouse preadinocyte cell line. It	
				is a continuous substrain of	
				2T2 Etractications	
				313 fibroblast cells developed	
				through clonal isolation. Cells	
				were differentiated to an	
				adipose-like state before being	
				used in the screen. See Green	
				H and Meuth M., Cell 3: 127-	
				133 (1974), which is herein	
				incorporated by reference in its	
				entirety.	
1	HNHOD46	1340	IL-10 in Human T-		
392			cell 2B9		
	HNHOD46	1340	SEAP in Jurkat-		
392			AP1		
	HNHOD46	1340	Activation of	Assays for the activation of	Preferred indications include
392			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
			response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
		•		(including antibodies and	infectious disease as described
			-	agonists or antagonists of the	below under "Infectious
		<del></del>		invention) to increase cAMP,	Disease"). Preferred
				bind to CREB transcription	indications include
		J		factor, and modulate	autoimmune diseases (e.g.,
				expression of genes involved	rheumatoid arthritis, systemic

	in a wide variety of cell	lupus erythematosis, multiple
-	functions. Exemplary assays	sclerosis and/or as described
	for transcription through the	below), immunodeficiencies
	cAMP response element that	(e.g., as described below),
_	may be used or routinely	boosting a T cell-mediated
	modified to test cAMP-	immune response, and
	response element activity of	suppressing a T cell-mediated
	polypeptides of the invention	immune response. Additional
	(including antibodies and	preferred indications include
	agonists or antagonists of the	inflammation and
	invention) include assays	inflammatory disorders.
	disclosed in Berger et al., Gene	Highly preferred indications
	66:1-10 (1998); Cullen and	include neoplastic diseases
	Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
	216:362-368 (1992); Henthorn	and/or as described below
	et al., Proc Natl Acad Sci USA	under "Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Genes 15(2):105-117	indications include neoplasms
	(1997); and Belkowski et al., J	and cancers, such as, leukemia,
	Immunol 161(2):659-665	lymphoma (e.g., T cell
	(1998), the contents of each of	lymphoma, Burkitt's
	which are herein incorporated	lymphoma, non-Hodgkins
	by reference in its entirety. T	lymphoma, Hodgkin"s
	cells that may be used	disease), melanoma, and
	according to these assays are	prostate, breast, lung, colon,
	publicly available (e.g.,	pancreatic, esophageal,
	through the ATCC).	stomach, brain, liver and
	Exemplary human T cells that	urinary cancer. Other preferred
	may be used according to these	indications include benign
	assays include the JURKAT	dysproliferative disorders and
	cell line, which is a suspension	pre-neoplastic conditions, such

				culture of leukemia cells that produce IL-2 when stimulated.	as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia
					(ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
					suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and afferey
392	HNHOD46	1340	Activation of transcription through NFAT response in immune	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-
			cells (such as T-cells).	are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the	Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases
				invention (including antibodies and agonists or antagonists of the invention) to regulate  NFAT transcription factors and	(e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below),

	modulate expression of genes	immunodeficiencies (e.g., as
	involved in	described below), boosting a T
	immunomodulatory functions.	cell-mediated immune
	Exemplary assays for	response, and suppressing a T
	transcription through the	cell-mediated immune
	NFAT response element that	response. Additional highly
	may be used or routinely	preferred indications include
	modified to test NFAT-	inflammation and
	response element activity of	inflammatory disorders. An
	polypeptides of the invention	additional highly preferred
	(including antibodies and	indication is infection (e.g., an
	agonists or antagonists of the	infectious disease as described
	invention) include assays	below under "Infectious
	disclosed in Berger et al., Gene	Disease"). Preferred
	66:1-10 (1998); Cullen and	indications include neoplastic
	Malm, Methods in Enzymol	diseases (e.g., leukemia,
	216:362-368 (1992); Henthorn	lymphoma, and/or as described
	et al., Proc Natl Acad Sci USA	below under
	85:6342-6346 (1988); Serfling	"Hyperproliferative
	et al., Biochim Biophys Acta	Disorders"). Preferred
	1498(1):1-18 (2000); De Boer	indications include neoplasms
	et al., Int J Biochem Cell Biol	and cancers, such as, for
-	31(10):1221-1236 (1999);	example, leukemia, lymphoma,
	Fraser et al., Eur J Immunol	and prostate, breast, lung,
	29(3):838-844 (1999); and	colon, pancreatic, esophageal,
	Yeseen et al., J Biol Chem	stomach, brain, liver and
	268(19):14285-14293 (1993),	urinary cancer. Other preferred
	the contents of each of which	indications include benign
	are herein incorporated by	dysproliferative disorders and
	reference in its entirety. T	pre-neoplastic conditions, such
	cells that may be used	as, for example, hyperplasia,

				according to these assays are publicly available (e.g., through the ATCC).  Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, supression of immune
					reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
392	HNHOD46	1340	Activation of transcription through NFKB response element in immune cells (such as basophils).	This reporter assay measures activation of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation of transcription through the NFKB response element are	Highly preferred indication includes allergy, asthma, and rhinitis. Additional highly preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease")
				well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	and inflammation and inflammatory disorders.  Preferred indications include immunological and hempatopoietic disorders (e.g.,

as described below under "Immune Activity", and "Blood-Related Disorders").  Preferred indications also	include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis,	multiple scierosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications also include	neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hynernroliferative	Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast. Jung. colon. pancreatic.	esophageal, stomach, brain, liver, urinary tract cancers and as described below under "Hyperproliferative Disorders".
agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of	immunomodulatory genes. Exemplary assays for transcription through the	NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention	(including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66.1-10 (1998). Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Marone et al. Int Arch Allergy Imminol 114(3):207-17	which are herein incorporated by reference in its entirety.  Basophils that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human basophil

				cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basonhils.	
392	HNHOD46	1340	Activation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkin's lymphoma, non-Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative
				GAS-response element activity of polypeptides of the invention (including antibodies	disorders and pre-neoplastic conditions, such as, for example, hyperplasia,

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	metaplasia, and/or dysplasia.	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., viral	infections, tuberculosis,	infections associated with	chronic granulomatosus	disease and malignant	osteoporosis, and/or an	infectious disease as described	below under "Infectious	Disease"). An additional	nreferred indication is
	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the MOLT4 cell line,	that may be used according to	these assays are publicly	available (e.g., through the	ATCC).										
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					idiopathic pulmonary fibrosis.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
			-		sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HNHOD46	1340	Activation of	Assays for the activation of	Highly preferred indications
392			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
			•	(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,

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multiple sclerosis and/or as	described below), and   immunodeficiencies (e.g., as	described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.
Exemplary assays for transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,	such as the MOLT4, that may	be used according to these	assays are publicly available	(e.g., through the ATCC).			
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		_																										

include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth, related
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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	HNHOD46
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genes in many cell types.  Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of	preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma,
	which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and

malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	cardiac repertusion injury, and
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					is infection (e.g., an infectious disease as described below
	HNHOD46	1340	Activation of	Assays for the activation of	Highly preferred indications
392			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as natural killer	to assess the ability of	as described below under
			cells).	polypeptides of the invention	"Immune Activity", "Blood-
	_			(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
		-		invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases
				modulate expression of	(e.g., rheumatoid arthritis,
				immunomodulatory genes.	systemic lupus erythematosis,
				Exemplary assays for	multiple sclerosis and/or as
		- 1,1		transcription through the	described below), and
				NFKB response element that	immunodeficiencies (e.g., as
				may be used or rountinely	described below). An
_				modified to test NFKB-	additional highly preferred
				response element activity of	indication is infection (e.g.,
				polypeptides of the invention	AIDS, and/or an infectious
				(including antibodies and	disease as described below
				agonists or antagonists of the	under "Infectious Disease").
				invention) include assays	Highly preferred indications
				disclosed in Berger et al., Gene	include neoplastic diseases
			-	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
				Malm, Methods in Enzymol	lymphoma, and/or as described
			-	216:362-368 (1992); Henthorn	below under
				et al., Proc Natl Acad Sci USA	"Hyperproliferative

	85:6342-6346 (1988): Valle	Disorders") Highly preferred
	Blazquez et al. Immunology	indications include neonlasms
	90(3):455-460 (1997);	and cancers, such as, for
	Aramburau et al., J Exp Med	example, melanoma, renal cell
	82(3):801-810 (1995); and	carcinoma, leukemia,
	Fraser et al., 29(3):838-844	lymphoma, and prostate,
	(1999), the contents of each of	breast, lung, colon, pancreatic,
	which are herein incorporated	esophageal, stomach, brain,
	by reference in its entirety.	liver and urinary cancer. Other
	NK cells that may be used	preferred indications include
	according to these assays are	benign dysproliferative
	publicly available (e.g.,	disorders and pre-neoplastic
	through the ATCC).	conditions, such as, for
	Exemplary human NK cells	example, hyperplasia,
	that may be used according to	metaplasia, and/or dysplasia.
	these assays include the NKL	Preferred indications also
	cell line, which is a human	include anemia, pancytopenia,
	natural killer cell line	leukopenia, thrombocytopenia,
	established from the peripheral	Hodgkin's disease, acute
	blood of a patient with large	lymphocytic anemia (ALL),
	granular lymphocytic	plasmacytomas, multiple
-	leukemia. This IL-2 dependent	myeloma, Burkitt's lymphoma,
	suspension culture cell line has	arthritis, AIDS, granulomatous
	a morphology resembling that	disease, inflammatory bowel
	of activated NK cells.	disease, sepsis, neutropenia,
		neutrophilia, psoriasis,
		hemophilia, hypercoagulation,
		diabetes mellitus, endocarditis,
-		meningitis, Lyme Disease,
		suppression of immune
		reactions to transplanted

					organs, asthma and allergy.
	HNHOD46	1340	Activation of	Assays for the activation of	Preferred indications
392			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are well-	(e.g., as described below under
			response element in	known in the art and may be	"Hyperproliferative
			immune cells (such	used or routinely modified to	Disorders"), blood disorders
			as T-cells).	assess the ability of	(e.g., as described below under
				polypeptides of the invention	"Immune Activity",
				(including antibodies and	"Cardiovascular Disorders",
				agonists or antagonists of the	and/or "Blood-Related
				invention) to modulate growth	Disorders"), and infection
				and other cell functions.	(e.g., an infectious disease as
				Exemplary assays for	described below under
				transcription through the AP1	"Infectious Disease"). Highly
				response element that may be	preferred indications include
				used or routinely modified to	autoimmune diseases (e.g.,
				test AP1-response element	rheumatoid arthritis, systemic
				activity of polypeptides of the	lupus erythematosis, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below) and
				the invention) include assays	immunodeficiencies (e.g., as
				disclosed in Berger et al., Gene	described below). Additional
				66:1-10 (1988); Cullen and	highly preferred indications
				Malm, Methods in Enzymol	include inflammation and
				216:362-368 (1992); Henthorn	inflammatory disorders.
				et al., Proc Natl Acad Sci USA	Highly preferred indications
				85:6342-6346 (1988);	also include neoplastic
				Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
				272(49):30806-30811 (1997);	lymphoma, and/or as described
				Chang et al., Mol Cell Biol	below under
				18(9):4986-4993 (1998); and	"Hyperproliferative

				Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are	Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia,
				herein incorporated by reference in its entirety. Human T cells that may be	lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,
				used according to these assays are publicly available (e.g.,	liver, and urinary cancer. Other preferred indications include
				through the ATCC).  Exemplary human T cells that	benign dysproliferative disorders and pre-neoplastic
				assays include the SUPT cell	example, hyperplasia,
				line, which is an IL-2 and IL-4 responsive suspension-culture	metaplasia, and/or dysplasia. Preferred indications include
				cell line.	arthritis, asthma, AIDS,
					allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression of
					immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HNHOD46	1340	Activation of	Assays for the activation of	A highly preferred
392			transcription	transcription through the CD28	embodiment of the invention
			through CD28	response element are well-	includes a method for

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stimulating T cell proliferation. An alternative highly preferred embodiment of the invention	includes a method for inhibiting T cell proliferation.	A highly preferred	includes a method for	activating T cells. An	alternative highly preferred	embodiment of the invention includes a method for	inhibiting the activation of	and/or inactivating T cells.	A highly preferred	embodiment of the invention	includes a method for		IL-2 production. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting (e.g.,	reducing) IL-2 production.	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,
known in the art and may be used or routinely modified to assess the ability of	polypeptides of the invention (including antibodies and	agonists or antagonists of the	expression in T cells.	Exemplary assays for	transcription through the CD28	response element that may be used or routinely modified to	test CD28-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	McGuire and Iacobelli, J	Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	3(1):552-560 (1998), the	contents of each of which are	herein incorporated by
response element in immune cells (such as T-cells).													.,	-											
			148																						
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		reference in its entirety. T	multiple sclerosis and/or as
		cells that may be used	described below),
		according to these assays are	immunodeficiencies (e.g., as
		publicly available (e.g.,	described below), boosting a T
		through the ATCC).	cell-mediated immune
		Exemplary human T cells that	response, and suppressing a T
		may be used according to these	cell-mediated immune
		assays include the SUPT cell	response. Highly preferred
		line, which is a suspension	indications include neoplastic
		culture of IL-2 and IL-4	diseases (e.g., melanoma, renal
		responsive T cells.	cell carcinoma, leukemia,
			lymphoma, and/or as described
	-		below under
			"Hyperproliferative
			Disorders"). Highly preferred
			indications include neoplasms
			and cancers, such as, for
			example, melanoma (e.g.,
			metastatic melanoma), renal
-	•		cell carcinoma (e.g., metastatic
			renal cell carcinoma),
			leukemia, lymphoma (e.g., T
			cell lymphoma), and prostate,
			breast, lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other
			preferred indications include
			benign dysproliferative
			disorders and pre-neoplastic
			conditions, such as, for
			example, hyperplasia,

metaplasia, and/or dysplasia. A highly preferred indication	includes infection (e.g., AIDS, tuberculosis, infections	associated with granulomatous	disease, and osteoporosis,	under "Infectious Disease"). A	highly preferred indication is	AIDS. Additional highly	preferred indications include	suppression of immune	reactions to transplanted	organs and/or tissues, uveitis,	psoriasis, and tropical spastic	paraparesis. Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, granulomatous	disease, inflammatory bowel
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					disease, sepsis, neutropenia.
					neutrophilia, hemophilia,
	712				hypercoagulation, diabetes
	****				mellitus, endocarditis,
					meningitis, Lyme Disease,
				The state of the s	asthma and allergy.
000	HNHOD46	1340	Activation of	Assays for the activation of	Highly preferred indications
392			transcription	transcription through the	include neoplastic diseases
			through GAS	Gamma Interferon Activation	(e.g., leukemia, lymphoma,
			response element in	Site (GAS) response element	and/or as described below
			immune cells (such	are well-known in the art and	under "Hyperproliferative
			as T-cells).	may be used or routinely	Disorders"). Highly preferred
				modified to assess the ability	indications include neoplasms
				of polypeptides of the	and cancers, such as, for
				invention (including antibodies	example, leukemia, lymphoma
				and agonists or antagonists of	(e.g., T cell lymphoma,
				the invention) to regulate	Burkitt's lymphoma, non-
				STAT transcription factors and	Hodgkins lymphoma,
				modulate gene expression	Hodgkin"s disease),
				involved in a wide variety of	melanoma, and prostate,
				cell functions. Exemplary	breast, lung, colon, pancreatic,
				assays for transcription	esophageal, stomach, brain,
				through the GAS response	liver and urinary cancer. Other
			•	element that may be used or	preferred indications include
				routinely modified to test	benign dysproliferative
				GAS-response element activity	disorders and pre-neoplastic
				of polypeptides of the	conditions, such as, for
				invention (including antibodies	example, hyperplasia,
				and agonists or antagonists of	metaplasia, and/or dysplasia.
				the invention) include assays	Preferred indications include
		77		disclosed in Berger et al., Gene	autoimmune diseases (e.g.,

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rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) immunodeficiencies	(e.g., as described below), boosting a T cell-mediated immune response, and	suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and	inflammatory disorders. Highly preferred indications include blood disorders (e.g.,	as described below under "Immune Activity", "Blood-	Related Disorders", and/or "Cardiovascular Disorders"),	and infection (e.g., viral infections, tuberculosis,	infections associated with chronic granulomatosus	disease and malignant osteoporosis, and/or an	infectious disease as described below under "Infectious	Disease"). An additional	idiopathic pulmonary fibrosis.	Preferred indications include
66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al. Proc Natl Acad Sci 11SA	85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and	Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by	Exemplary human T cells, such as the SUPT cell line, that	may be used according to these assays are publicly available	(e.g., through the ATCC).							
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leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.	Assays for the activation of transcription through the stranscription through the cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies invention) to regulate involved in multiple sclerosis and/or as well-known in the art and may be used or routinely modified to assess the ability preferred indications include autoimmune diseases invention) to regulate systemic lupus erythematosis, the invention factors and described below), multiple sclerosis and/or as described below), boosting a Timmunomodulatory functions.
	Activation of transcription through NFAT response element in immune cells (such as T-cells).
	1340
	HNHOD46
	392

cell-mediated immune response. Additional highly preferred indications include inflammation and	inflammatory disorders. An additional highly preferred indication is infection (e.g., an infection disorders)	below under "Infectious Disease"), Preferred indications include neoplastic	diseases (e.g., leukemia, lymphoma, and/or as described below under	Hyperpronneranve Disorders"). Preferred indications include neoplasms	and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung,	colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia.
transcription through the NFAT response element that may be used or routinely modified to test NFAT-	response element activity of polypeptides of the invention (including antibodies and	agomsts or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and	Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	62:0342-0340 (1988); Serting et al., Biochim Biophys Acta 1498(1):1-18 (2000); De Boer	et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol	29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which	are herein incorporated by reference in its entirety. T cells that may be used	according to these assays are publicly available (e.g., through the ATCC).

Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	
may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that
	Activation of transcription through NFKB response element in immune cells (such as T-cells).
	1340
	HNHOD46
	392

	may be used or rountinely	described below). An
-	modified to test NFKB-	additional highly preferred
	response element activity of	indication is infection (e.g.,
 	polypeptides of the invention	AIDS, and/or an infectious
 	(including antibodies and	disease as described below
 	agonists or antagonists of the	under "Infectious Disease").
	invention) include assays	Highly preferred indications
	disclosed in Berger et al., Gene	include neoplastic diseases
	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
 	Malm, Methods in Enzymol	lymphoma, and/or as described
 	216:362-368 (1992); Henthorn	below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Gnes 15(2):105-117	indications include neoplasms
	(1997); and Fraser et al.,	and cancers, such
 	29(3):838-844 (1999), the	as,melanoma, renal cell
	contents of each of which are	carcinoma, leukemia,
	herein incorporated by	lymphoma, and prostate,
 	reference in its entirety. T	breast, lung, colon, pancreatic,
 	cells that may be used	esophageal, stomach, brain,
 	according to these assays are	liver and urinary cancer. Other
	publicly available (e.g.,	preferred indications include
 	through the ATCC).	benign dysproliferative
	Exemplary human T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,
	line, which is a suspension	metaplasia, and/or dysplasia.
	culture of IL-2 and IL-4	Preferred indications also
 	responsive T cells.	include anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute

					lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted
392	HNHOD46	1340	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6 transcription factors and modulate the expression of multiple genes. Exemplary assays for transcription	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic

	element that may be used or	lupus erythematosis, multiple
	 routinely modified to test	sclerosis and/or as described
	STAT6 response element	below) and
	 activity of the polypeptides of	immunodeficiencies (e.g., as
	 the invention (including	described below).
-	antibodies and agonists or	Preferred indications include
	antagonists of the invention)	neoplastic diseases (e.g.,
	include assays disclosed in	leukemia, lymphoma,
	Berger et al., Gene 66:1-10	melanoma, and/or as described
	(1998); Cullen and Malm,	below under
	Methods in Enzymol 216:362-	"Hyperproliferative
	368 (1992); Henthorn et al.,	Disorders"). Preferred
	Proc Natl Acad Sci USA	indications include neoplasms
	85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
-	 et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
	(1998); Moffatt et al.,	prostate, breast, lung, colon,
	Transplantation 69(7):1521-	pancreatic, esophageal,
	1523 (2000); Curiel et al., Eur	stomach, brain, liver and
	J Immunol 27(8):1982-1987	urinary cancer. Other preferred
	(1997); and Masuda et al., J	indications include benign
	 Biol Chem 275(38):29331-	dysproliferative disorders and
	29337 (2000), the contents of	pre-neoplastic conditions, such
	 each of which are herein	as, for example, hyperplasia,
	incorporated by reference in its	metaplasia, and/or dysplasia.
	entirety. T cells that may be	Preferred indications include
	 used according to these assays	anemia, pancytopenia,
	are publicly available (e.g.,	leukopenia, thrombocytopenia,
	 through the ATCC).	Hodgkin's disease, acute
	Exemplary T cells that may be	lymphocytic anemia (ALL),
	used according to these assays	plasmacytomas, multiple
	include the SUPT cell line,	myeloma, Burkitt's lymphoma.

				of IL-2 and IL-4 responsive T cells.	disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious
393	HNHOG73	1341	SEAP in 293/ISRE		Disease").
393	HNHOG73	1341	Activation of transcription through cAMP response element (CRE) in preadipocytes.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP, regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell	A highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease

	functions. For example, a	nephropathy and/or other
	3T3-L1/CRE reporter assay	diseases and disorders as
	may be used to identify factors	described in the "Renal
 	that activate the cAMP	Disorders" section below),
 	signaling pathway. CREB	diabetic neuropathy, nerve
	plays a major role in	disease and nerve damage
	adipogenesis, and is involved	(e.g., due to diabetic
	in differentiation into	neuropathy), blood vessel
	adipocytes. CRE contains the	blockage, heart disease, stroke,
	binding sequence for the	impotence (e.g., due to diabetic
	transcription factor CREB	neuropathy or blood vessel
	(CRE binding protein).	blockage), seizures, mental
	Exemplary assays for	confusion, drowsiness,
	transcription through the	nonketotic hyperglycemic-
 	cAMP response element that	hyperosmolar coma,
 	may be used or routinely	cardiovascular disease (e.g.,
	modified to test cAMP-	heart disease, atherosclerosis,
	response element activity of	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
 	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in Berger et al., Gene	section below), dyslipidemia,
	66:1-10 (1998); Cullen and	endocrine disorders (as
	Malm, Methods in Enzymol	described in the "Endocrine
	216:362-368 (1992); Henthorn	Disorders" section below),
	et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
	85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
	et al., Mol Cell Biol	blindness), ulcers and impaired
	20(3):1008-1020 (2000); and	wound healing, and infection
	Klemm et al., J Biol Chem	(e.g., infectious diseases and

			273:917-923 (1998), the contents of each of which are berein incorporated by	disorders as described in the "Infectious Diseases" section
			reference in its entirety. Pre-	below, especially of the urinary tract and skin), carpal
			adipocytes that may be used	tunnel syndrome and
			according to these assays are	Dupuytren's contracture).
			through the ATCC) and/or	indications are complications
			may be routinely generated.	associated with insulin
			Exemplary mouse adipocyte	resistance.
			cells that may be used	
			according to these assays	
			include 3T3-L1 cells. 3T3-L1	
			is an adherent mouse	
			preadipocyte cell line that is a	
			continuous substrain of 3T3	
			fibroblast cells developed	
•••			through clonal isolation and	
•			undergo a pre-adipocyte to	
			adipose-like conversion under	
217			appropriate differentiation	
	,		conditions known in the art.	
HNHOG73	1341	Activation of	This reporter assay measures	Highly preferred indication
		transcription	activation of the NFkB	includes allergy, asthma, and
		through NFKB	signaling pathway in Ku812	rhinitis. Additional highly
		response element in	human basophil cell line.	preferred indications include
		immune cells (such	Assays for the activation of	infection (e.g., an infectious
		as basophils).	transcription through the	disease as described below
			NFKB response element are	under "Infectious Disease"),
			well-known in the art and may	and inflammation and
			be used or routinely modified	inflammatory disorders.

Preferred indications include	immunological and	hempatopoietic disorders (e.g.,	as described below under	"Immune Activity", and	"Blood-Related Disorders").	Preferred indications also	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,		below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative	Disorders".
to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	et al, Int Arch Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Basophils that may be used	according to these assays are
											Asses	***	- 141																	
			noraa																-										******	

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis.
publicly available (e.g., through the ATCC).  Exemplary human basophil cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
	1341
	HNHOG73
	393

	modified to test SRE activity	systemic lunus erythematosis
0	of the polypeptides of the	Crohn"s disease, multiple
<u>.:i</u>	invention (including antibodies	sclerosis and/or as described
	and agonists or antagonists of	below), immunodeficiencies
<u>中</u>	the invention) include assays	(e.g., as described below),
<u>p</u>	disclosed in Berger et al., Gene	boosting a T cell-mediated
9	66:1-10 (1998); Cullen and	immune response, and
2	Malm, Methods in Enzymol	suppressing a T cell-mediated
2	216:362-368 (1992); Henthorn	immune response. Additional
<u> </u>	et al., Proc Natl Acad Sci USA	highly preferred indications
 <u> </u>	85:6342-6346 (1988); Benson	include inflammation and
et	et al., J Immunol 153(9):3862-	inflammatory disorders, and
35	3873 (1994); and Black et al.,	treating joint damage in
<u> </u>	Virus Genes 12(2):105-117	patients with rheumatoid
<u>(1)</u>	(1997), the content of each of	arthritis. An additional highly
<u> </u>	which are herein incorporated	preferred indication is sepsis.
	by reference in its entirety. T	Highly preferred indications
3	cells that may be used	include neoplastic diseases
<u>ac</u>	according to these assays are	(e.g., leukemia, lymphoma,
<u>d</u>	publicly available (e.g.,	and/or as described below
	through the ATCC).	under "Hyperproliferative
 <u> </u>	Exemplary T cells that may be	Disorders"). Additionally,
in	used according to these assays	highly preferred indications
<u> </u>	include the NK-YT cell line,	include neoplasms and
M	which is a human natural killer	cancers, such as, for example,
<u> </u>	cell line with cytolytic and	leukemia, lymphoma,
<u>ව</u>	cytotoxic activity.	melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,

					liver and uringry cancer Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
				•	metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
-					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HNHPD10	1342	Activation of	Assays for the activation of	A highly preferred indication

394		transcription	transcription through the	is obesity and/or complications
		through cAMP	cAMP response element are	associated with obesity
		rachonca alaman		Additional highly macfaunal
		Icaponise elenient		Additional ingilly preferred
		(CRE) in pre-	be used or routinely modified	indications include weight loss
		adipocytes.	to assess the ability of	or alternatively, weight gain.
			polypeptides of the invention	An additional highly preferred
			including antibodies and	indication is diabetes mellitus.
	-		agonists or antagonists of the	An additional highly preferred
			invention) to increase cAMP,	indication is a complication
			regulate CREB transcription	associated with diabetes (e.g.,
			factors, and modulate	diabetic retinopathy, diabetic
			expression of genes involved	nephropathy, kidney disease
			in a wide variety of cell	(e.g., renal failure,
			functions. For example, a	nephropathy and/or other
			3T3-L1/CRE reporter assay	diseases and disorders as
			may be used to identify factors	described in the "Renal
	-		that activate the cAMP	Disorders" section below),
	-		signaling pathway. CREB	diabetic neuropathy, nerve
			plays a major role in	disease and nerve damage
			adipogenesis, and is involved	(e.g., due to diabetic
			in differentiation into	neuropathy), blood vessel
			adipocytes. CRE contains the	blockage, heart disease, stroke,
			binding sequence for the	impotence (e.g., due to diabetic
			transcription factor CREB	neuropathy or blood vessel
			(CRE binding protein).	blockage), seizures, mental
			Exemplary assays for	confusion, drowsiness,
			transcription through the	nonketotic hyperglycemic-
			cAMP response element that	hyperosmolar coma,
		-	may be used or routinely	cardiovascular disease (e.g.,
•			modified to test cAMP-	heart disease, atherosclerosis,
			response element activity of	microvascular disease,

		And the state of t	polypeptides of the invention	hypertension, stroke, and other
			(including antibodies and	diseases and disorders as
			agonists or antagonists of the	described in the
			invention) include assays	"Cardiovascular Disorders"
			disclosed in Berger et al., Gene	section below), dyslipidemia,
			66:1-10 (1998); Cullen and	endocrine disorders (as
			Malm, Methods in Enzymol	described in the "Endocrine
			216:362-368 (1992); Henthorn	Disorders" section below),
			et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
			85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
	••		et al., Mol Cell Biol	blindness), ulcers and impaired
			20(3):1008-1020 (2000); and	wound healing, and infection
			Klemm et al., J Biol Chem	(e.g., infectious diseases and
			273:917-923 (1998), the	disorders as described in the
			contents of each of which are	"Infectious Diseases" section
			herein incorporated by	below, especially of the
			reference in its entirety. Pre-	urinary tract and skin), carpal
			adipocytes that may be used	tunnel syndrome and
			according to these assays are	Dupuytren's contracture).
			publicly available (e.g.,	Additional highly preferred
			through the ATCC) and/or	indications are complications
-1			may be routinely generated.	associated with insulin
-			Exemplary mouse adipocyte	resistance.
			cells that may be used	
			according to these assays	
			include 3T3-L1 cells. 3T3-L1	
			is an adherent mouse	
			preadipocyte cell line that is a	
			continuous substrain of 3T3	
			fibroblast cells developed	
			through clonal isolation and	

			undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	
HNHPD10	1342	SEAP in HIB/CRE		
HNHPD10	1342	Activation of	This reporter assay measures	Highly preferred indications
		transcription	activation of the GATA-3	include allergy, asthma, and
		through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
		response element in	human mast cell line.	indications include infection
		immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
		as mast cells).	cells has been linked to	described below under
			cytokine and chemokine	"Infectious Disease"), and
			production. Assays for the	inflammation and
			activation of transcription	inflammatory disorders.
		- San Face	through the GATA3 response	Preferred indications also
			element are well-known in the	include blood disorders (e.g.,
			art and may be used or	as described below under
			routinely modified to assess	"Immune Activity", "Blood-
			the ability of polypeptides of	Related Disorders", and/or
			the invention (including	"Cardiovascular Disorders").
			antibodies and agonists or	Preferred indications include
			antagonists of the invention) to	autoimmune diseases (e.g.,
			regulate GATA3 transcription	rheumatoid arthritis, systemic
			factors and modulate	lupus erythematosis, multiple
			expression of mast cell genes	sclerosis and/or as described
			important for immune response	below) and
			development. Exemplary	immunodeficiencies (e.g., as
		•	assays for transcription	described below). Preferred
			through the GATA3 response	indications include neoplastic
			element that may be used or	diseases (e.g., leukemia,

	routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
	invention (including antibodies	
	and agonists or antagonists of	
	the invention) include assays	described below under
	disclosed in Berger et al., Gene	
	66:1-10 (1998); Cullen and	
	Malm, Methods in Enzymol	
	216:362-368 (1992); Henthorn	
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	et al., Cold Spring Harb Symp	
	Quant Biol 64:563-571 (1999);	
	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
	Cell 89(4):587-596 (1997); and	
	Henderson et al., Mol Cell Biol	
	14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
,	contents of each of which are	lymphoma, arthritis, AIDS,
	herein incorporated by	granulomatous disease,
	reference in its entirety. Mast	inflammatory bowel disease,
	cells that may be used	sepsis, neutropenia,
	according to these assays are	neutrophilia, psoriasis,
	publicly available (e.g.,	suppression of immune
	through the ATCC).	reactions to transplanted
	Exemplary human mast cells	organs and tissues, hemophilia,
	that may be used according to	hypercoagulation, diabetes
	these assays include the HMC-	mellitus, endocarditis,
	1 cell line, which is an	meningitis, and Lyme Disease.

	Highly preferred indications include alleroy asthma and	rhinitis. Additional preferred	indications include infection	(e.g., an infectious disease as	"Infectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,
immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	This reporter assay measures activation of the NFAT	signaling pathway in HMC-1	human mast cell line.	Activation of NFAT in mast cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the Nuclear Factor of	Activated T cells (NFAT)	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the
	Activation of transcription	through NFAT	response element in	mmune cells (such	`											MATE.							
	1342						-					•											
	HNHPD10																						
·	394		•																				

NFAT response element that	Ivmphome melenome
mon to med an anti1-	iyinpilolila, ilicialibilla,
 may be used or routinely	prostate, breast, lung, colon,
modified to test NFAT-	pancreatic, esophageal,
response element activity of	stomach, brain, liver, and
polypeptides of the invention	urinary tract cancers and/or as
 (including antibodies and	described below under
agonists or antagonists of the	"Hyperproliferative
invention) include assays	Disorders"). Other preferred
disclosed in Berger et al., Gene	indications include benign
 66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
 85:6342-6346 (1988); De Boer	Preferred indications include
et al., Int J Biochem Cell Biol	anemia, pancytopenia,
31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et al., J Immunol	leukemias, Hodgkin's disease,
165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
al., J Exp Med 188:527-537	granulomatous disease,
(1998), the contents of each of	inflammatory bowel disease,
which are herein incorporated	sepsis, neutropenia,
by reference in its entirety.	neutrophilia, psoriasis,
Mast cells that may be used	suppression of immune
according to these assays are	reactions to transplanted
publicly available (e.g.,	organs and tissues, hemophilia,
through the ATCC).	hypercoagulation, diabetes
Exemplary human mast cells	mellitus, endocarditis,
that may be used according to	meningitis, and Lyme Disease.

				these assays include the HMC-1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HNTBI57	1343	Activation of	This reporter assay measures	Highly preferred indications
395			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
<u> </u>				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
-				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred

		191	through the GATA3 response	indications include neonlastic
			element that may be used or	diseases (e.g., leukemia
			routinely modified to test	lymphoma, melanoma.
	٠		GATA3-response element	prostate, breast, lung, colon,
			activity of polypeptides of the	pancreatic, esophageal,
			invention (including antibodies	stomach, brain, liver, and
			and agonists or antagonists of	urinary tract cancers and/or as
			the invention) include assays	described below under
			disclosed in Berger et al., Gene	"Hyperproliferative
			66:1-10 (1998); Cullen and	Disorders"). Other preferred
_			Malm, Methods in Enzymol	indications include benign
			216:362-368 (1992); Henthorn	dysproliferative disorders and
			et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
			85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
			et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
			Quant Biol 64:563-571 (1999);	Preferred indications include
			Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
			J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
			(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
			Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
			Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
			14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
			contents of each of which are	lymphoma, arthritis, AIDS,
			herein incorporated by	granulomatous disease,
			reference in its entirety. Mast	inflammatory bowel disease,
			cells that may be used	sepsis, neutropenia,
			according to these assays are	neutrophilia, psoriasis,
			publicly available (e.g.,	suppression of immune
			through the ATCC).	reactions to transplanted
			Exemplary human mast cells	organs and tissues, hemophilia,
	1		that may be used according to	hypercoagulation, diabetes

(e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating ioint damage in	patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative	Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for
and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and	invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890	(1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art.
	<u> </u>	

				Human dendritic cells are	example, hyperplasia,
				antigen presenting cells in	metaplasia, and/or dysplasia.
				suspension culture, which,	Preferred indications include
				when activated by antigen	anemia, pancytopenia,
				and/or cytokines, initiate and	leukopenia, thrombocytopenia,
				upregulate T cell proliferation	Hodgkin's disease, acute
				and functional activities.	lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
396	HNTCE26	1344	CD69 in Human T cells		
	HNTCE26	1344	Stimulation of	Assays for measuring secretion	A highly preferred
396			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preterred
			beta cells.	routinely modified to assess	indication is a complication

	the obility of mountained	7 - 1 - 1 - 1 - 1 - 7 - 7
	the author of pulpeptides of	associated with diabetes (e.g.,
	the invention (including	diabetic retinopathy, diabetic
	antibodies and agonists or	nephropathy, kidney disease
	antagonists of the invention) to	(e.g., renal failure,
	stimulate insulin secretion.	nephropathy and/or other
	For example, insulin secretion	diseases and disorders as
	is measured by FMAT using	described in the "Renal
	anti-rat insulin antibodies.	Disorders" section below),
	Insulin secretion from	diabetic neuropathy, nerve
	pancreatic beta cells is	disease and nerve damage
	upregulated by glucose and	(e.g., due to diabetic
	also by certain	neuropathy), blood vessel
	proteins/peptides, and	blockage, heart disease, stroke,
	disregulation is a key	impotence (e.g., due to diabetic
	component in diabetes.	neuropathy or blood vessel
	Exemplary assays that may be	blockage), seizures, mental
	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Ahren, B., et al.,	diseases and disorders as
	Am J Physiol, 277(4 Pt	described in the
	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
	al., Endocrinology,	section below), dyslipidemia,
	138(9):3735-40 (1997); Kim,	endocrine disorders (as
 	K.H., et al., FEBS Lett,	described in the "Endocrine
	377(2):237-9 (1995); and,	Disorders" section below),
	Miraglia S et. al., Journal of	neuropathy, vision impairment

				Biomolecular Screening	(e o diahetic retinonathy and
				4:193-204 (1999), the contents	blindness), ulcers and impaired
				of each of which is herein	wound healing, and infection
				incorporated by reference in its	(e.g., infectious diseases and
-				entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
				assays are publicly available	below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
				pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
		-		pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
(	HNTCE26	1344	Production of	Assays for measuring	Preferred embodiments of the
396			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of

Inflammation, Vascular Disease, Athereosclerosis,											S										A highly preferred	embodiment of the invention	includes a method for	stimulating adipocyte		highly preferred embodiment	of the invention includes a	method for inhibiting	adipocyte proliferation. A
agonists or antagonists of the invention) to regulate ICAM-1	expression. Exemplary assays	that may be used or routinely	modified to measure ICAM-1	expression include assays	disclosed in: Takacs P, et al,	FASEB J, 15(2):279-281	(2001); and, Miyamoto K, et	al., Am J Pathol, 156(5):1733-	1739 (2000), the contents of	each of which is herein	incorporated by reference in its	entirety. Cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary cells that may be	used according to these assays	include microvascular	endothelial cells (MVEC).	Kinase assay. Kinase assays,	for example an Elk-1 kinase	assay, for ERK signal	transduction that regulate cell	proliferation or differentiation	are well known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the
																				-	Activation of	Adipocyte ERK	Signaling Pathway						
			81-81			_															1345								
									-												HNTNC20								
	•	•									-											397							

invention (including antibodies	highly preferred embodiment
and agonists or antagonists of	of the invention includes a
 the invention) to promote or	method for stimulating
inhibit cell proliferation,	adipocyte differentiation. An
activation, and differentiation.	alternative highly preferred
Exemplary assays for ERK	embodiment of the invention
kinase activity that may be	includes a method for
 used or routinely modified to	inhibiting adipocyte
test ERK kinase-induced	differentiation. A highly
activity of polypeptides of the	preferred embodiment of the
invention (including antibodies	invention includes a method
and agonists or antagonists of	for stimulating (e.g.,
the invention) include the	increasing) adipocyte
assays disclosed in Forrer et	activation. An alternative
al., Biol Chem 379(8-9):1101-	highly preferred embodiment
1110 (1998); Le Marchand-	of the invention includes a
Brustel Y, Exp Clin	method for inhibiting the
Endocrinol Diabetes	activation of (e.g., decreasing)
107(2):126-132 (1999);	and/or inactivating adipocytes.
Kyriakis JM, Biochem Soc	Highly preferred indications
Symp 64:29-48 (1999); Chang	include endocrine disorders
and Karin, Nature	(e.g., as described below under
410(6824):37-40 (2001); and	"Endocrine Disorders").
Cobb MH, Prog Biophys Mol	Highly preferred indications
Biol 71(3-4):479-500 (1999);	also include neoplastic
the contents of each of which	diseases (e.g., lipomas,
are herein incorporated by	liposarcomas, and/or as
 reference in its entirety.	described below under
Mouse adipocyte cells that	"Hyperproliferative
may be used according to these	Disorders"). Preferred
assays are publicly available	indications include blood

disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural	disorders (e.g., as described	below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve
(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.																
		_																											

(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or
							_												• • •											
														-										-						

complications associated with obesity. Additional highly preferred indications include weight loss or alternatively.	weight gain. Additional highly preferred indications are complications associated with insulin resistance.	Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies,	muscular dystrophy, and/or as described herein. Additional highly preferred indications include,	hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating	disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms	and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred	indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain,

397 HNTNC20 HNTNI01 398				IIvei, allu milialy calleel.
				Highly preferred indications
				include lipomas and
				liposarcomas. Other preferred
				indications include benign
				dysproliferative disorders and
				pre-neoplastic conditions, such
				as, for example, hyperplasia,
				metaplasia, and/or dysplasia.
	1345	TNFa in Human T-cell 2B9		
398	1346	Regulation of	Assays for the regulation of	A highly preferred indication
		transcription via	transcription through the	is diabetes mellitus.
		DMEF1 response	DMEF1 response element are	Additional highly preferred
		element in	well-known in the art and may	indications include
		adipocytes and pre-	be used or routinely modified	complications associated with
	,	adipocytes	to assess the ability of	diabetes (e.g., diabetic
			polypeptides of the invention	retinopathy, diabetic
			(including antibodies and	nephropathy, kidney disease
			agonists or antagonists of the	(e.g., renal failure,
			invention) to activate the	nephropathy and/or other
			DMEF1 response element in a	diseases and disorders as
			reporter construct (such as that	described in the "Renal
			containing the GLUT4	Disorders" section below),
			promoter) and to regulate	diabetic neuropathy, nerve
			insulin production. The	disease and nerve damage
			DMEF1 response element is	(e.g., due to diabetic
			present in the GLUT4	neuropathy), blood vessel
			promoter and binds to MEF2	blockage, heart disease, stroke,
			transcription factor and another	impotence (e.g., due to diabetic
			transcription factor that is	neuropathy or blood vessel

ulation blockage), seizures, mental skeletal confusion, drowsiness, primary nonketotic hyperglycemicose hyperosmolar coma, uscle cardiovascular disease (e.g.,	that F1			blindness), ulcers and impaired blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and of a 30- disorders as described in the	ment "Infectious Diseases" section below, especially of the urinary tract and skin). An additional highly preferred		weight loss or alternatively,   weight gain. Additional highly
required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle	tissue. Exemplary assays that may be used or routinely modified to test for DMEF1 response element activity (in	adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies) and agonists or antagonists of	the invention) include assays disclosed in Thai, M.V., et al., J Biol Chem, 273(23):14285-92	Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21 (1994); "Identification of a 30-	base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in	transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al.,	Methods in Enzymol. 216:362–368 (1992), the

				contents of each of which is	preferred indications are
-				herein incorporated by	complications associated with
				reference in its entirety.	insulin resistance.
_	,,,,,	-		Adipocytes and pre-adipocytes	
				that may be used according to	
				these assays are publicly	
_				available (e.g., through the	
				ATCC) and/or may be	
				routinely generated.	
				Exemplary cells that may be	
·•				used according to these assays	
				include the mouse 3T3-L1 cell	
				line which is an adherent	
				mouse preadipocyte cell line.	
				Mouse 3T3-L1 cells are a	
				continuous substrain of 3T3	
				fibroblasts developed through	
				clonal isolation. These cells	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
	-			appropriate differentiation	
,				culture conditions.	
٠	HNTNI01	1346	Activation of	Assays for the activation of	A highly preferred indication
398			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred

invention) to increase cAMP.	indication is a complication
regulate CREB transcription	associated with diabetes (e.g.,
factors, and modulate	diabetic retinopathy, diabetic
expression of genes involved	nephropathy, kidney disease
 in a wide variety of cell	(e.g., renal failure,
functions. For example, a	nephropathy and/or other
3T3-L1/CRE reporter assay	diseases and disorders as
may be used to identify factors	described in the "Renal
that activate the cAMP	Disorders" section below),
 signaling pathway. CREB	diabetic neuropathy, nerve
plays a major role in	disease and nerve damage
adipogenesis, and is involved	(e.g., due to diabetic
in differentiation into	neuropathy), blood vessel
adipocytes. CRE contains the	blockage, heart disease, stroke,
binding sequence for the	impotence (e.g., due to diabetic
transcription factor CREB	neuropathy or blood vessel
 (CRE binding protein).	blockage), seizures, mental
Exemplary assays for	confusion, drowsiness,
transcription through the	nonketotic hyperglycemic-
 cAMP response element that	hyperosmolar coma,
may be used or routinely	cardiovascular disease (e.g.,
modified to test cAMP-	heart disease, atherosclerosis,
response element activity of	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
 (including antibodies and	diseases and disorders as
agonists or antagonists of the	described in the
invention) include assays	"Cardiovascular Disorders"
 disclosed in Berger et al., Gene	section below), dyslipidemia,
66:1-10 (1998); Cullen and	endocrine disorders (as
   Malm, Methods in Enzymol	described in the "Endocrine
216:362-368 (1992); Henthorn	Disorders" section below),

				i ilearopatiiv, visioli iliiballillelli
			85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
			et al., Mol Cell Biol	blindness), ulcers and impaired
			20(3):1008-1020 (2000); and	wound healing, and infection
		· ·	Klemm et al., J Biol Chem	(e.g., infectious diseases and
			273:917-923 (1998), the	disorders as described in the
	•		contents of each of which are	"Infectious Diseases" section
			herein incorporated by	below, especially of the
			reference in its entirety. Pre-	urinary tract and skin), carpal
			adipocytes that may be used	tunnel syndrome and
			according to these assays are	Dupuytren's contracture).
			publicly available (e.g.,	Additional highly preferred
			through the ATCC) and/or	indications are complications
			may be routinely generated.	associated with insulin
-	4		Exemplary mouse adipocyte	resistance.
			cells that may be used	
			according to these assays	
			include 3T3-L1 cells. 3T3-L1	
			is an adherent mouse	
			preadipocyte cell line that is a	
			continuous substrain of 3T3	
			fibroblast cells developed	
			through clonal isolation and	
			undergo a pre-adipocyte to	
			adipose-like conversion under	
			appropriate differentiation	
Con trade to the h			conditions known in the art.	
HNINI0]	1346	Activation of	Assays for the activation of	A highly preferred indication
398		transcription	transcription through the	is obesity and/or complications
		through serum	Serum Response Element	associated with obesity.
		response element in	(SRE) are well-known in the	Additional highly preferred

routinely modified to assess and may be used or routinely modified to assess and modulate the distriction is diabetes mellitus.  The ability of polypeptides of an additional highly preferred antagonists of the invention including the serum response in growth. Exemplary assays for transcription through the rephropathy, diabetic expression of genes involved (e.g., renal failure, for transcription through the sphropathy, kidney disease in growth. Exemplary assays)  Factors and modulate the diabetic returnship, sidney disease in growth. Exemplary assays to the phypaptides of phypaptides of phypaptides of the invention including the invention including antagonists or the invention including the invention including antagonists or the invention including the escribed in the "Renal antagonists of the invention" phypaptides of p	[x		<del></del>		0	<u> </u>
pre-adipocytes.	indications include weight los or alternatively, weight gain. An additional highly preferred indication is diabetes mellitus.	An additional mgmy preserved indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nenhronathy, kidney disease	(e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal	Disorders" section below), diabetic neuropathy, nerve disease and nerve damage	neuropathy), blood vessel blockage, heart disease, stroke impotence (e.g., due to diabeti neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma,	cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and othe diseases and disorders as described in the
	art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved	in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE	activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention)	include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes	12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Preadipocytes that may be used according to these assays are
2403	pre-adipocytes.	·····				
2403						
	<u> </u>			2403	3	

				publicly available (e.g.,	"Cardiovascular Disorders"
				through the ATCC) and/or	section below), dyslinidemia.
				may be routinely generated.	endocrine disorders (as
				Exemplary mouse adipocyte	described in the "Endocrine
				cells that may be used	Disorders" section below),
_				according to these assays	neuropathy, vision impairment
_				include 3T3-L1 cells. 3T3-L1	(e.g., diabetic retinopathy and
				is an adherent mouse	blindness), ulcers and impaired
		,		preadipocyte cell line that is a	wound healing, and infection
				continuous substrain of 3T3	(e.g., infectious diseases and
				fibroblast cells developed	disorders as described in the
				through clonal isolation and	"Infectious Diseases" section
				undergo a pre-adipocyte to	below). Additional highly
-				adipose-like conversion under	preferred indications are
				appropriate differentiation	complications associated with
				conditions known in the art.	insulin resistance.
	HNTNI01	1346	Activation of	Assays for the activation of	Highly preferred indications
398			transcription	transcription through the	include asthma, allergy,
			through GAS	Gamma Interferon Activation	hypersensitivity reactions,
			response element in	Site (GAS) response element	inflammation, and
-			immune cells (such	are well-known in the art and	inflammatory disorders.
			as eosinophils).	may be used or routinely	Additional highly preferred
				modified to assess the ability	indications include immune
				of polypeptides of the	and hematopoietic disorders
		-		invention (including antibodies	(e.g., as described below under
				and agonists or antagonists of	"Immune Activity", and
				the invention) to modulate	"Blood-Related Disorders"),
				gene expression (commonly	autoimmune diseases (e.g.,
				via STAT transcription factors)	rheumatoid arthritis, systemic
-				involved in a wide variety of	lupus erythematosis, Crohn's
				cell functions. Exemplary	disease, multiple sclerosis

and/or as described below),	immunodeficiencies (e.g., as	described below), boosting an	eosinophil-mediated immune	response and, alternatively,	suppressing an eosinophil-	mediated immune response.																								
assays for transcription	through the GAS response	element that may be used or	routinely modified to test	GAS-response element activity	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Matikainen et al., Blood	93(6):1980-1991 (1999); and	Henttinen et al., J Immunol	155(10):4582-4587 (1995); the	contents of each of which are	herein incorporated by	reference in its entirety.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to activate or	inhibit activation of immune	cells include assays disclosed
				,	,							,					,													

and/or cited in: Mavumi M	"EoL-1, a human eosinophilic	cell line" Leuk Lymphoma;	Jun;7(3):243-50 (1992);	Bhattacharya S, "Granulocyte	macrophage colony-	stimulating factor and	interleukin-5 activate STAT5	and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Respir Cell	Mol Biol; Mar;24(3):312-6	(2001); and, Du J, et al.,	"Engagement of the CrkL	adapter in interleukin-5	signaling in eosinophils" J Biol	Chem; Oct 20;275(42):33167-	75 (2000); the contents of each	of which are herein	incorporated by reference in its	entirety. Exemplary cells that	may be used according to these	assays include eosinophils.	Eosinophils are a type of	immune cell important in the	late stage of allergic reactions;	they are recruited to tissues	and mediate the inflammtory	response of late stage allergic	reaction. Increases in GAS	mediated transcription in
						,	•	-				-	_		_										-	-	-	•	_	
															24														,	

lly a result normally a of sytokine (e.g. IL3,	1		nent are hypersensitivity reactions, and and may inflammation preferred		of (e.g., an infectious disease as		s and "Infectious Disease"),		e NFKB   inflammation and	and inflammatory disorders (e.g.,	of as described below under				hat	tinely   rheumatoid arthritis, systemic				s and immunodeficiencies (e.g., as	sts of the described below).	ssays	et al., Gene	len and
of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3,			through NFKB  NFKB response element are response element are			polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and
	1346 Activation of	transcription	through NFKB response eleme	immune c	as EOL1 cells).		-					-		-			•							
	HNTNI01	398				· -	-																	

Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology	90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844	(1999), the contents of each of which are herein incorporated by reference in its entirety.	For example, a reporter assay (which measures increases in transcription inducible from a NEB responsive element in	EOL-1 cells) may link the NFKB element to a repeorter gene and binds to the NFKB transcription factor, which is	upregulated by cytokines and other factors. Exemplary immune cells that may be used according to these assays	include eosinophils such as the human EOL-1 cell line of eosinophils. Eosinophils are a type of immune cell important	in the allergic responses; they are recruited to tissues and mediate the inflammtory

				response of late stage allergic	
				reaction. Eol-1 is a human	
				eosinophil cell line.	
	HNTN101	1346	Regulation of	Assays for the regulation of	A highly preferred
398	_		transcription of	transcription of Malic Enzyme	indication is diabetes mellitus.
			Malic Enzyme in	are well-known in the art and	An additional highly preferred
			adipocytes	may be used or routinely	indication is a complication
				modified to assess the ability	associated with diabetes (e.g.,
	-12		_	of polypeptides of the	diabetic retinopathy, diabetic
				invention (including antibodies	nephropathy, kidney disease
			•	and agonists or antagonists of	(e.g., renal failure,
				the invention) to regulate	nephropathy and/or other
				transcription of Malic Enzyme,	diseases and disorders as
				a key enzyme in lipogenesis.	described in the "Renal
				Malic enzyme is involved in	Disorders" section below),
_				lipogenesisand its expression is	diabetic neuropathy, nerve
•		4		stimulted by insulin. ME	disease and nerve damage
- 44				promoter contains two direct	(e.g., due to diabetic
				repeat (DR1)- like elements	neuropathy), blood vessel
		.,		MEp and MEd identified as	blockage, heart disease, stroke,
				putative PPAR response	impotence (e.g., due to diabetic
				elements. ME promoter may	neuropathy or blood vessel
				also responds to AP1 and other	blockage), seizures, mental
				transcription factors.	confusion, drowsiness,
	_		_	Exemplary assays that may be	nonketotic hyperglycemic-
				used or routinely modified to	hyperosmolar coma,
				test for regulation of	cardiovascular disease (e.g.,
				transcription of Malic Enzyme	heart disease, atherosclerosis,
				(in adipoocytes) by	microvascular disease,
				polypeptides of the invention	hypertension, stroke, and other
				(including antibodies and	diseases and disorders as

				agonists or antagonists of the	described in the
····				invention) include assays	"Cardiovascular Disorders"
				disclosed in: Streeper, R.S., et	section below), dyslipidemia,
•				al., Mol Endocrinol,	endocrine disorders (as
				12(11):1778-91 (1998);	described in the "Endocrine
	-			Garcia-Jimenez, C., et al., Mol	Disorders" section below),
				Endocrinol, 8(10):1361-9	neuropathy, vision impairment
				(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
				Biol Chem, 274(25):17997-	blindness), ulcers and impaired
				8004 (1999); Ijpenberg, A., et	wound healing, and infection
				al., J Biol Chem,	(e.g., infectious diseases and
				272(32):20108-20117 (1997);	disorders as described in the
				Berger, et al., Gene 66:1-10	"Infectious Diseases" section
				(1988); and, Cullen, B., et al.,	below, especially of the
				Methods in Enzymol.	urinary tract and skin), carpal
				216:362–368 (1992), the	tunnel syndrome and
-				contents of each of which is	Dupuytren's contracture).
				herein incorporated by	An additional highly preferred
				reference in its entirety.	indication is obesity and/or
				Hepatocytes that may be used	complications associated with
	<b></b>		···	according to these assays are	obesity. Additional highly
				publicly available (e.g.,	preferred indications include
				through the ATCC) and/or	weight loss or alternatively,
				may be routinely generated.	weight gain. Aditional
				Exemplary hepatocytes that	highly preferred indications are
	_		-	may be used according to these	complications associated with
				assays includes the H4IIE rat	insulin resistance.
				liver hepatoma cell line.	
	HNTNI01	1346	Activation of	This reporter assay measures	Highly preferred indications
398			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred

	response element in	human mast cell line.	indications include infection
	immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
	as mast cells).	cells has been linked to	described below under
-		cytokine and chemokine	"Infectious Disease"), and
		production. Assays for the	inflammation and
		activation of transcription	inflammatory disorders.
		through the GATA3 response	Preferred indications also
		element are well-known in the	include blood disorders (e.g.,
		art and may be used or	as described below under
		routinely modified to assess	"Immune Activity", "Blood-
		the ability of polypeptides of	Related Disorders", and/or
		the invention (including	"Cardiovascular Disorders").
		antibodies and agonists or	Preferred indications include
		antagonists of the invention) to	autoimmune diseases (e.g.,
-		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
		expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and
_		development. Exemplary	immunodeficiencies (e.g., as
		assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
-		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
		the invention) include assays	described below under
	-	disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign

		·		216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions, such
				85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
				et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
				Quant Biol 64:563-571 (1999);	Preferred indications include
				Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
				J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
				(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
			***	these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HNTNI01	1346	Activation of	This reporter assay measures	Highly preferred indications
398			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred

	response element in	human mast cell line.	indications include infection
	immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
	as mast cells).	cells has been linked to	described below under
		cytokine and chemokine	"Infectious Disease"), and
		production. Assays for the	inflammation and
		activation of transcription	inflammatory disorders.
		through the Nuclear Factor of	Preferred indications also
		Activated T cells (NFAT)	include blood disorders (e.g.,
-		response element are well-	as described below under
		known in the art and may be	"Immune Activity", "Blood-
		used or routinely modified to	Related Disorders", and/or
		assess the ability of	"Cardiovascular Disorders").
		polypeptides of the invention	Preferred indications include
-		(including antibodies and	autoimmune diseases (e.g.,
		agonists or antagonists of the	rheumatoid arthritis, systemic
		invention) to regulate NFAT	lupus erythematosis, multiple
		transcription factors and	sclerosis and/or as described
		modulate expression of genes	below) and
		involved in	immunodeficiencies (e.g., as
		immunomodulatory functions.	described below). Preferred
		Exemplary assays for	indications include neoplastic
		transcription through the	diseases (e.g., leukemia,
		NFAT response element that	lymphoma, melanoma,
		may be used or routinely	prostate, breast, lung, colon,
		modified to test NFAT-	pancreatic, esophageal,
		response element activity of	stomach, brain, liver, and
		polypeptides of the invention	urinary tract cancers and/or as
		(including antibodies and	described below under
		agonists or antagonists of the	"Hyperproliferative
		invention) include assays	Disorders"). Other preferred
		disclosed in Berger et al., Gene	indications include benign

			66:1-10 (1998); Cullen and	dysproliferative disorders and
	1		Malm, Methods in Enzymol	pre-neoplastic conditions, such
			216:362-368 (1992); Henthorn	as, for example, hyperplasia,
			et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
			85:6342-6346 (1988); De Boer	Preferred indications include
			et al., Int J Biochem Cell Biol	anemia, pancytopenia,
			31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	na 1		et al., J Immunol	leukemias, Hodgkin's disease,
			165(12):7215-7223 (2000);	acute lymphocytic anemia
		***	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
			Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
			16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
			al., J Exp Med 188:527-537	granulomatous disease,
			(1998), the contents of each of	inflammatory bowel disease,
			which are herein incorporated	sepsis, neutropenia,
			by reference in its entirety.	neutrophilia, psoriasis,
			Mast cells that may be used	suppression of immune
			according to these assays are	reactions to transplanted
			publicly available (e.g.,	organs and tissues, hemophilia,
			through the ATCC).	hypercoagulation, diabetes
			Exemplary human mast cells	mellitus, endocarditis,
			that may be used according to	meningitis, and Lyme Disease.
			these assays include the HMC-	
			1 cell line, which is an	
			immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HNTNI01	1346	Activation of	This reporter assay measures	Highly preferred indication

				66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA	example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,
				85:6342-6346 (1988); Stassen et al, J Immunol 166(7):4391-8 (2001); and Marquardt and Walker, J Allergy Clin	liver, urinary tract cancers and as described below under "Hyperproliferative Disorders".
				the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used	
				according to these assays are publicly available (e.g., through the ATCC).	
	·			Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an	
				immature human mast cell line established from the peripheral blood of a patient with mast	
				cell leukemia, and exhibits many characteristics of immature mast cells.	
	HNTNI01	1346	Activation of	Assays for the activation of	Highly preferred indications
			through STAT6	transcription through the Signal Transducers and	include allergy, asthma, and rhinitis. Additional highly
			response element in	Activators of Transcription	preferred indications include
-			immune cents (such	(51A16) response element in	infection (e.g., an infectious

		as mast cells).	immune cells (such as in the	disease as described below
			human HMC-1 mast cell line)	under "Infectious Disease"),
			are well-known in the art and	and inflammation and
-	V-1	-	may be used or routinely	inflammatory disorders.
			modified to assess the ability	Preferred indications also
			of polypeptides of the	include hematopoietic and
			invention (including antibodies	immunological disorders (e.g.,
			and agonists or antagonists of	as described below under
			the invention) to regulate	"Immune Activity", "Blood-
			STAT6 transcription factors	Related Disorders", and/or
_			and modulate the expression of	"Cardiovascular Disorders"),
			multiple genes. Exemplary	autoimmune diseases (e.g.,
			assays for transcription	rheumatoid arthritis, systemic
-			through the STAT6 response	lupus erythematosis, multiple
			element that may be used or	sclerosis and/or as described
24			routinely modified to test	below), and
			STAT6 response element	immunodeficiencies (e.g., as
			activity of the polypeptides of	described below). Preferred
			the invention (including	indications include neoplastic
			antibodies and agonists or	diseases (e.g., leukemia,
			antagonists of the invention)	lymphoma, melanoma, and/or
			include assays disclosed in	as described below under
	-		Berger et al., Gene 66:1-10	"Hyperproliferative
	-		(1998); Cullen and Malm,	Disorders"). Preferred
			Methods in Enzymol 216:362-	indications include neoplasms
			368 (1992); Henthorn et al.,	and cancer, such as, for
•••			Proc Natl Acad Sci USA	example, leukemia, lymphoma,
			85:6342-6346 (1988);	melanoma, and prostate,
			Sherman, Immunol Rev	breast, lung, colon, pancreatic,
			179:48-56 (2001); Malaviya	esophageal, stomach, brain,
			and Uckun, J Immunol	liver and urinary cancer. Other

				168:421-426 (2002); Masuda	preferred indications include
_		-		et al., J Biol Chem	benign dysproliferative
				275(38):29331-29337 (2000);	disorders and pre-neoplastic
				and Masuda et al., J Biol Chem	conditions, such as, for
				276:26107-26113 (2001), the	example, hyperplasia,
-	-			contents of each of which are	metaplasia, and/or dysplasia.
				herein incorporated by	Preferred indications include
				reference in its entirety. Mast	hematopoietic and
				cells that may be used	immunological disorders such
				according to these assays are	as arthritis, AIDS,
,				publicly available (e.g.,	granulomatous disease,
				through the ATCC).	inflammatory bowel disease,
				Exemplary human mast cells	sepsis, neutropenia,
				that may be used according to	neutrophilia, psoriasis,
				these assays include the HMC-	suppression of immune
				1 cell line, which is an	reactions to transplanted
				immature human mast cell line	organs and tissues, hemophilia,
				established from the peripheral	hypercoagulation, diabetes
				blood of a patient with mast	mellitus, endocarditis,
			-	cell leukemia, and exhibits	meningitis, and Lyme Disease.
				many characteristics of	
	, V. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1.	,		immature mast cells.	
900	HNINI01	1346	Activation of	This reporter assay measures	Highly preferred indication
398			transcription	activation of the NFkB	includes allergy, asthma, and
			through NFKB	signaling pathway in Ku812	rhinitis. Additional highly
			response element in	human basophil cell line.	preferred indications include
			immune cells (such	Assays for the activation of	infection (e.g., an infectious
			as basophils).	transcription through the	disease as described below
				NFKB response element are	under "Infectious Disease"),
				well-known in the art and may	and inflammation and
				be used or routinely modified	inflammatory disorders.

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ions incl	pun	disorders	ow under	ty", and	Disorder	ions also	nune dise	1 arthritis	rythemat	s and/or	and (	cies (e.g.,	). Preferi	include	es (e.g.,	oma,	or as desc		ive	ferred	de neopla	as, for	iia, lympl	rostate,	n, pancre	nach, bra	ct cancers	w under	ive
Preferred indications include	immunological and	hempatopoietic disorders (e.g.,	as described below under	"Immune Activity", and	"Blood-Related Disorders").	Preferred indications also	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancer, such as, for	example, leukemia, lymphoma,	melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary tract cancers and	as described below under	"Hyperproliferative
Prefer	immu	hemps	as des	ımmı,	"Bloo	Prefer	includ	(e.g., 1	systen	multip	descril	immm	descril	indica	neopla	leuken	melan	below	"Hype	Disord	indicat	and ca	examb	melan	breast,	esopha	liver, 1	as desc	"Hvpe
	ention	pu	of the	<b>VFKB</b>	q	ći i	nes.		ıe	ıt that	ely	ı	ty of	ention	pu	of the	ys	I., Gene	and	ymol	enthorn	ci USA	Marone		7	each of	orated	ety.	ised
bility of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	ays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Marone	Allergy	Immunol 114(3):207-17	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Basophils that may be used
to assess the ability of	eptides o	ding anti	sts or ant	tion) to r	ription fa	late expr	nomodul	Exemplary assays for	ription tl	3 respons	e used o	ied to tes	se elem	eptides o	ding anti	sts or ant	ion) incl	sed in Be	0 (1998)	, Method	25-368	Proc Nat	42-6346	et al, Int Arch Allergy	nol 114(	), the cor	are here	erence in	hils that
to ass	polyp	(inclu	agonis	invent	transc	modn	immn	Exem	transc	NFKE	may b	modif	respor	polype	(inclu	agonis	invent	disclo	66:1-1	Malm	216:30	et al.,	85:63	et al, I	Immu	(1997)	which	by refe	Basop
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-			-																										

				publicly available (e.g.,	
				through the ATCC).	
				Exemplary human basophil	
				cell lines that may be used	
				according to these assays	
				include Ku812, originally	
				established from a patient with	
				chronic myelogenous	
				leukemia. It is an immature	
				prebasophilic cell line that can	
	-			be induced to differentiate into	
				mature basophils.	
	HNTNI01	1346	SEAP in		n-reported.
398			Molt4/SRE		
	HNTNI01	1346	Activation of	Assays for the activation of	Highly preferred indications
398			transcription	transcription through the	include blood disorders (e.g.,
			through NFAT	Nuclear Factor of Activated T	as described below under
	-		response element in	cells (NFAT) response element	"Immune Activity", "Blood-
			immune cells (such	are well-known in the art and	Related Disorders", and/or
			as natural killer	may be used or routinely	"Cardiovascular Disorders").
			cells).	modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
				NFAT transcription factors and	described below),
		. 1151		modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				- Control - Cont	

response. Additional highly preferred indications include inflammation and	inflammatory disorders. An additional highly preferred	indication is infection (e.g., an infections disease as described	below under "Infectious	Disease"). Preferred	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute
NFAT response element that may be used or routinely modified to test NFAT-	response element activity of polypeptides of the invention	(including antibodies and	invention) include assays	disclosed in Berger et al., Gene	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Aramburu et al., J Exp Med	182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. NK	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to
							-																		
							-														-				
						_	_								· · · · ·										

,				these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
398	HNTNI01	1346	SEAP in NK16/STAT6		
398	INTNIOI I	1346	Activation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, melanoma, and prostate, melanoma, and prostate, breast, lung, colon, pancreatic,

		assavs for transcription	econhageal etomoch brain
		thurst the CAS manner	1: 1 :
		unough the GAS response	liver and urinary cancer. Other
		element that may be used or	preferred indications include
		routinely modified to test	benign dysproliferative
	-	GAS-response element activity	disorders and pre-neoplastic
		of polypeptides of the	conditions, such as, for
		invention (including antibodies	example, hyperplasia,
		and agonists or antagonists of	metaplasia, and/or dysplasia.
	-	the invention) include assays	Preferred indications include
		disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
		66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
		Malm, Methods in Enzymol	lupus erythematosis, multiple
		216:362-368 (1992); Henthorn	sclerosis and/or as described
		et al., Proc Natl Acad Sci USA	below), immunodeficiencies
		85:6342-6346 (1988);	(e.g., as described below),
-		Matikainen et al., Blood	boosting a T cell-mediated
		93(6):1980-1991 (1999); and	immune response, and
		Henttinen et al., J Immunol	suppressing a T cell-mediated
		155(10):4582-4587 (1995), the	immune response. Additional
		contents of each of which are	preferred indications include
-		herein incorporated by	inflammation and
		reference in its entirety.	inflammatory disorders.
		Exemplary human T cells,	Highly preferred indications
		such as the SUPT cell line, that	include blood disorders (e.g.,
		may be used according to these	as described below under
		assays are publicly available	"Immune Activity", "Blood-
-		(e.g., through the ATCC).	Related Disorders", and/or
			"Cardiovascular Disorders"),
			and infection (e.g., viral
			infections, tuberculosis,
			infections associated with

chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and alleroy.	
	Kinase assay. Kinase assays, cle Cell for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the
	Skeletal Mucle Cell PI3 Kinase Signalling Pathway
	HNTSY18 1347
	399

į		art and may be used or	includes a method for
		routinely modified to assess	decreasing muscle cell
		the ability of polypeptides of	survival. A preferred
		the invention (including	embodiment of the invention
		antibodies and agonists or	includes a method for
		antagonists of the invention) to	stimulating muscle cell
		promote or inhibit glucose	proliferation. In a specific
		metabolism and cell survival.	embodiment, skeletal muscle
		Exemplary assays for PI3	cell proliferation is stimulated.
		kinase activity that may be	An alternative highly preferred
		used or routinely modified to	embodiment of the invention
		test PI3 kinase-induced activity	includes a method for
		of polypeptides of the	inhibiting muscle cell
		invention (including antibodies	proliferation. In a specific
		and agonists or antagonists of	embodiment, skeletal muscle
		the invention) include assays	cell proliferation is inhibited.
		disclosed in Forrer et al., Biol	A preferred embodiment of
		Chem 379(8-9):1101-1110	the invention includes a
		(1998); Nikoulina et al.,	method for stimulating muscle
		Diabetes 49(2):263-271	cell differentiation. In a
		(2000); and Schreyer et al.,	specific embodiment, skeletal
		Diabetes 48(8):1662-1666	muscle cell differentiation is
		(1999), the contents of each of	stimulated. An alternative
		which are herein incorporated	highly preferred embodiment
		by reference in its entirety.	of the invention includes a
	-	Rat myoblast cells that may be	method for inhibiting muscle
		used according to these assays	cell differentiation. In a
		are publicly available (e.g.,	specific embodiment, skeletal
		through the ATCC).	muscle cell differentiation is
		Exemplary rat myoblast cells	inhibited. Highly preferred
		that may be used according to	indications include disorders of

the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative	Disorders"), endocrine disorders (e.g., as described below under "Endocrine Disorders"), neural disorders	(e.g., as described below under "Neural Activity and Neurological Diseases"), blood	disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-	Related Disorders"), immune disorders (e.g., as described below under "Immune	fection  w under se"). ndication	diabetes mellitus.  additional highly preferred indication is a complication associated with diabetes (e.g.,	nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other
these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuses to form	multinucleated myotubes and striated fibers after culture in differentiation media.						

diseases and disorders as described in the "Renal	Disorders" section below), diabetic neuropathy, nerve	disease and nerve damage (e.g.,	due to diabetic neuropathy),	blood vessel blockage, neart disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infections	(e.g., infectious diseases and	disorders as described in the
											-													,		_	

				1	below under
				-	"Hyperproliferative
				I	Disorders"). Highly preferred
				· <del>-</del>	indications include neoplasms
		<del></del>			and cancers, such as, for
					example, melanoma (e.g.,
				1	metastatic melanoma), renal
	~				cell carcinoma (e.g., metastatic
				-	renal cell carcinoma),
					leukemia, lymphoma (e.g., T
					cell lymphoma), and prostate,
				<u>-</u>	breast, lung, colon, pancreatic,
-				_	esophageal, stomach, brain,
				_	liver and urinary cancer. Other
				<del></del>	preferred indications include
					benign dysproliferative
•	-				disorders and pre-neoplastic
	-				conditions, such as, for
7-7-				-	example, hyperplasia,
				<u> </u>	metaplasia, and/or dysplasia.
		<del></del>		7	A highly preferred indication
					includes infection (e.g.,
				_	AIDS, tuberculosis, infections
					associated with granulomatous
					disease, and osteoporosis,
-					and/or as described below
				<u></u>	under "Infectious Disease"). A
-					highly preferred indication is
				7	AIDS. Additional highly
		-11	<del></del>		preferred indications include
				S	suppression of immune

					reactions to transplanted
···					organs and/or tissues, uveitis,
					psoriasis, and tropical spastic
					paraparesis. Preferred
					indications include blood
					disorders (e.g., as described
					below under "Immune
					Activity", "Blood-Related
					Disorders", and/or
					"Cardiovascular Disorders").
			, 18		Preferred indications also
	_				include anemia, pancytopenia,
	-				leukopenia, thrombocytopenia,
				,	Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
	-				arthritis, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HOAAC90	1348	Activation of	Assays for the activation of	Highly preferred indications
400			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under

finelypeptides of the invention "Immune Activity", "Blood- finelying antibodies and Related Disorders" and/or	the			modulate expression of (e.g., rheumatoid arthritis,	immunomodulatory genes. systemic lupus erythematosis,	Exemplary assays for multiple sclerosis and/or as		NFKB response element that immunodeficiencies (e.g., as	may be used or rountinely described below). An	modified to test NFKB- additional highly preferred		polypeptides of the invention   AIDS, and/or an infectious	(including antibodies and disease as described below	agonists or antagonists of the under "Infectious Disease").	invention) include assays Highly preferred indications	disclosed in Berger et al., Gene   include neoplastic diseases	66:1-10 (1998); Cullen and (e.g., melanoma, leukemia,	Malm, Methods in Enzymol   lymphoma, and/or as described	216:362-368 (1992); Henthorn   below under	et al., Proc Natl Acad Sci USA   "Hyperproliferative	85:6342-6346 (1988); Black et   Disorders"). Highly preferred	al., Virus Gnes 15(2):105-117   indications include neoplasms	(1997); and Fraser et al., and cancers, such	29(3):838-844 (1999), the as,melanoma, renal cell	contents of each of which are carcinoma, leukemia,	herein incorporated by lymphoma, and prostate,	reference in its entirety. T breast, lung, colon, pancreatic,	cells that may be used esophageal, stomach, brain,	poorting to these reserve one lives and minour son or Other
od (ui)	age	invi	tra	om	mi	Ex	tra	EX.	ma	mo	res	od			ni	dis	99	Ma	210	et	85:	al,	(19	29(	100	her		lea	
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publicly available (e.g., through the ATCC).  Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension responsive T cells.	LL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgA production (IgA plays a loft in mucosal immunity).
publicly through t Exempla may be u assays in line, whi culture o responsiv	Production of IL-6 FM.  by T cell effects or participal IgE prod IgA prod role in m
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disorders. Additional highly preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	multiple myeloma, Burkitt's	lymphoma arthritic AIDS
may be used or routinely modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.	
						_													-				_				-		
					-	-						-						-					_						

					granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted
					organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
401	HOACB38	1349	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood vessels and are involved in	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hynemoroliferative Disorders"

				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
				endothelial cells (HUVEC),	esophageal, stomach, brain,
				which are available from	liver and urinary cancer. Other
				commercial sources. The	preferred indications include
				expression of VCAM	benign dysproliferative
				(CD106), a membrane-	disorders and pre-neoplastic
				associated protein, can be	conditions, such as, for
				upregulated by cytokines or	example, hyperplasia,
				other factors, and contributes	metaplasia, and/or dysplasia.
				to the extravasation of	
				lymphocytes, leucocytes and	
				other immune cells from blood	
				vessels; thus VCAM	
				expression plays a role in	
				promoting immune and	
				inflammatory responses.	
_	HOCNF19	1350	Activation of	Kinase assay. Kinase assays,	A highly preferred
402			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting

	of polypeptides of the	adipocyte proliferation. A
	invention (including antibodies	highly preferred embodiment
	and agonists or antagonists of	of the invention includes a
	the invention) to promote or	method for stimulating
	inhibit cell proliferation,	adipocyte differentiation. An
	activation, and differentiation.	alternative highly preferred
	Exemplary assays for ERK	embodiment of the invention
	kinase activity that may be	includes a method for
	used or routinely modified to	inhibiting adipocyte
	test ERK kinase-induced	differentiation. A highly
	activity of polypeptides of the	preferred embodiment of the
	invention (including antibodies	invention includes a method
	and agonists or antagonists of	for stimulating (e.g.,
	the invention) include the	increasing) adipocyte
 	assays disclosed in Forrer et	activation. An alternative
	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	1110 (1998); Le Marchand-	of the invention includes a
 	Brustel Y, Exp Clin	method for inhibiting the
	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	Disorders"). Preferred

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indications include blood disorders (e.g., hypertension, congestive heart failure, blood	stroke, impotence and/or as described below under "Immune Activity",	"Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders	"Immune Activity"), neural disorders (e.g., as described	below under "Neural Activity and Neurological Diseases"),	and infection (e.g., as described below under	"Infectious Disease"). A highly preferred indication	is diabetes mellitus. An additional highly preferred	indication is a complication	diabetic retinopathy, diabetic	nephropathy, kidney disease	re.g., renal familie, nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve
assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used	according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse	preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and	undergo a pre-adipocyte to adipose-like conversion under	appropriate differentiation conditions known in the art.											

disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred

			indication is obesity and/or
			complications associated with
			obesity. Additional highly
			preferred indications include
			weight loss or alternatively,
			weight gain. Additional
			highly preferred indications are
			complications associated with
			insulin resistance.
		-	Additional highly preferred
	-		indications are disorders of the
			musculoskeletal systems
			including myopathies,
			muscular dystrophy, and/or as
-			described herein.
			Additional highly preferred
			indications include,
			hypertension, coronary artery
			disease, dyslipidemia,
			gallstones, osteoarthritis,
			degenerative arthritis, eating
			disorders, fibrosis, cachexia,
			and kidney diseases or
			disorders. Preferred
			indications include neoplasms
			and cancer, such as,
		_	lymphoma, leukemia and
			breast, colon, and kidney
			cancer. Additional preferred
			indications include melanoma,
		-	prostate lino pancreatic

					esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include linemas and
					liposarcomas. Other preferred
					dysproliferative disorders and
					pre-neoplastic conditions, such as. for example, hyperplasia.
					metaplasia, and/or dysplasia.
402	HOCNF19	1350	HLA-DR in Human T cells		
	HOCNF19	1350	Production of IL-4	IL-4 FMAT. Assays for	A highly preferred
405				immunomodulatory proteins	embodiment of the invention
				secreted by TH2 cells that	includes a method for
				stimulate B cells, T cells,	stimulating (e.g., increasing)
		-		macrophages and mast cells	IL-4 production. An alternative
		~		and promote polarization of	highly preferred embodiment
				CD4+ cells into TH2 cells are	of the invention includes a
				well known in the art and may	method for inhibiting (e.g.,
				be used or routinely modified	reducing) IL-4 production.
				to assess the ability of	A highly preferred indication
				polypeptides of the invention	includes asthma. A highly
				(including antibodies and	preferred indication includes
				agonists or antagonists of the	allergy. A highly preferred
				invention) to mediate	indication includes rhinitis.
	-			immunomodulation, stimulate	Additional highly preferred
				immune cells, modulate	indications include
	· ·			immune cell polarization,	inflammation and
	-			and/or mediate humoral or	inflammatory disorders.
				cell-mediated immunity.	Highly preferred indications

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Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells.  Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194); Yssel et al., Res Immunol 1(3):257-261 (2000); and van der Graaff et al., Nat Immunol 1(3):257-261 (2000); he contents of each of which are	Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are	Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells.  Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (194); Yssel et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are	Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are	include neoplastic diseases	(e.g., leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Preferred	indications include neoplasms	and cancers, such as, for	example, leukemia, lymphon	melanoma, and prostate,	breast, lung, colon, pancreati	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic		lupus erythematosis, multiple
				Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-4, and	the stimulation of immune	cells, such as B cells, T cells,	macrophages and mast cells.	Such assays that may be used	or routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin	Lab Anal 8(5):277-283 (1194);	Yssel et al., Res Immunol	144(8):610-616 (1993); Bagley	et al., Nat Immunol 1(3):257-	261 (2000); and van der Graaff		38(3):214-220 (1999), the	contents of each of which are		herein incorporated by

				used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	immunodeficiencies (e.g., as described below). Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infectious described below under "Infectious Disease").
403	HODDF13	1351	Regulation of transcription through the FAS promoter element in hepatocytes	Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease

(e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below)	diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease,	hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below),	neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection
(including antibodies and agonists or antagonists of the invention) to activate the FAS promoter element in a reporter	transcription of FAS, a key enzyme for lipogenesis. FAS promoter is regulated by many transcription factors including SREBP. Insulin increases FAS gene transcription in livers of	diabetic mice. This stimulation of transcription is also somewhat glucose dependent. Exemplary assays that may be used or routinely modified to test for FAS promoter element activity (in hepatocytes) by polypeptides	of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Xiong, S., et al., Proc Natl Acad Sci U.S.A., 97(8):3948-53 (2000); Roder, K., et al., Eur J Biochem, 260(3):743-51	(1999); Oskoulan B, et al., Biochem J, 317 ( Pt 1):257-65 (1996); Berger, et al., Gene 66:1-10 (1988); and, Cullen,

				B., et al., Methods in Enzymol.	(e.g., infectious diseases and
					disorders as described in the
		-		contents of each of which is	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety.	urinary tract and skin), carpal
				Hepatocytes that may be used	tunnel syndrome and
				according to these assays, such	Dupuytren's contracture).
				as H4IIE cells, are publicly	An additional highly preferred
				available (e.g., through the	indication is obesity and/or
				ATCC) and/or may be	complications associated with
		,		routinely generated.	obesity. Additional highly
				Exemplary hepatocytes that	preferred indications include
	-			may be used according to these	weight loss or alternatively,
				assays include rat liver	weight gain. Aditional
		v		hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
	HODDF13	1351	Inhibition of	Reporter Assay: construct	
403			squalene synthetase	contains regulatory and coding	
			gene transcription.	sequence of squalene	
				synthetase, the first specific	
				enzyme in the cholesterol	
· · · ·				biosynthetic pathway. See	
				Jiang, et al., J. Biol. Chem.	
				268:12818-128241(993), the	
				contents of which are herein	
				incorporated by reference in its	
				entirety. Cells were treated	
				with SID supernatants, and	
				SEAP activity was measured	
				after 72 hours. HepG2 is a	

	Highly preferred indications include allergy, asthma, and	indications include infection	(e.g., an infectious disease as described below under	"Infectious Disease"), and	inflammation and	inflammatory disorders.	referred indications also include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic
human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	This reporter assay measures activation of the GATA-3	human mast cell line.	Activation of GA1A-3 in mast cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	Infough the GATA3 response element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate GATA3 transcription	factors and modulate	expression of mast cell genes	important for immune response	development. Exemplary	assays for transcription	through the GATA3 response
	Activation of transcription	response element in	as mast cells).																	
	1351																			
	HODDF13												-711-2	-						
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leukemia,	it, lung, colon	ophageal,	n, liver, and	ancers and/or	w under	rative	Other preferre	lude benign	e disorders an	conditions, su	e, hyperplasia	d/or dysplasia	cations includ	topenia,	rombocytopei	dgkin's disea	sytic anemia	acytomas,	oma, Burkitt's	thritis, AIDS,	s disease,	bowel disease	cnia,	osoriasis,	fimmune	ansplanted	sues, hemophi	ion, diabetes	carditis.
diseases (e.g., leukemia, lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,
element that may be used or routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	that may be used according to	these assays include the HMC-
elemen	GATA	activity	inventi	and ag	the inv	disclos	66:1-10	Malm,	216:36	et al., I	85:634	et al., (	Quant	Rodrig	J Immı	(1999)	Cell 86	Hendel	14(6):4	conten	herein	referen	cells th	accord	public	throug	Exemp	that me	these a
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				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HODDF13	1351	Activation of	This reporter assay measures	Highly preferred indications
403			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT .	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
		-		used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
	-			transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
				Exemplary assays for	indications include neoplastic

	transcription through the	diseases (e.g., leukemia,
	NFAT response element that	lymphoma, melanoma,
	may be used or routinely	prostate, breast, lung, colon,
	modified to test NFAT-	pancreatic, esophageal,
	response element activity of	stomach, brain, liver, and
	polypeptides of the invention	urinary tract cancers and/or as
	(including antibodies and	described below under
	agonists or antagonists of the	"Hyperproliferative
	invention) include assays	Disorders"). Other preferred
	disclosed in Berger et al., Gene	indications include benign
	66:1-10 (1998); Cullen and	dysproliferative disorders and
	Malm, Methods in Enzymol	pre-neoplastic conditions, such
	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
 	85:6342-6346 (1988); De Boer	Preferred indications include
	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
	31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
	et al., J Immunol	leukemias, Hodgkin's disease,
	165(12):7215-7223 (2000);	acute lymphocytic anemia
	Hutchinson and McCloskey, J	(ALL), plasmacytomas,
	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
	16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
	al., J Exp Med 188:527-537	granulomatous disease,
	(1998), the contents of each of	inflammatory bowel disease,
	which are herein incorporated	sepsis, neutropenia,
	by reference in its entirety.	neutrophilia, psoriasis,
	Mast cells that may be used	suppression of immune
	according to these assays are	reactions to transplanted
	publicly available (e.g.,	organs and tissues, hemophilia,
	through the ATCC).	hypercoagulation, diabetes
	Exemplary human mast cells	mellitus, endocarditis,

			that may be used according to these assays include the HMC-	meningitis, and Lyme Disease.
			I cell line, which is an immature human mast cell line	
			established from the peripheral	
			blood of a patient with mast	
			cell leukemia, and exhibits	
			many characteristics of	
			immature mast cells.	
HODDF13	1351	Production of	Assays for measuring	Highly preferred indications
		VCAM in	expression of VCAM are well-	include inflammation (acute
		endothelial cells	known in the art and may be	and chronic), restnosis,
		such as human	used or routinely modified to	atherosclerosis, asthma and
		umbilical vein	assess the ability of	allergy. Highly preferred
		endothelial cells	polypeptides of the invention	indications include
		(HUVEC))	(including antibodies and	inflammation and
			agonists or antagonists of the	inflammatory disorders,
	_		invention) to regulate VCAM	immunological disorders,
			expression. For example,	neoplastic disorders (e.g.
			FMAT may be used to meaure	cancer/tumorigenesis), and
			the upregulation of cell surface	cardiovascular disorders (such
			VCAM-1 expresssion in	as described below under
-			endothelial cells. Endothelial	"Immune Activity", "Blood-
			cells are cells that line blood	Related Disorders",
			vessels, and are involved in	"Hyperproliferative Disorders"
			functions that include, but are	and/or "Cardiovascular
			not limited to, angiogenesis,	Disorders"). Highly preferred
			vascular permeability, vascular	indications include neoplasms
			tone, and immune cell	and cancers such as, for
			extravasation. Exemplary	example, leukemia, lymphoma,
   	:		endothelial cells that may be	melanoma, renal cell

				used according to these assays include human umbilical vein endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membraneassociated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM	carcinoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
				expression plays a role in promoting immune and inflammatory responses.	
403	HODDF13	1351	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)		
403	HODDF13	1351	Activation of Transcription	Assays for activation of transcription are well-known in the art and may be used and routinely modified to assess	
				ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells	
				were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was	

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
measured after 48 hours. LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of specific tumoral markers in colon cancer. See, Patan et al., Circ Res, 89(8):732-39 (2001), the contents of which are herein incorporated by reference in its entirety.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of
	Production of ICAM-1
	1352
	HODDN65
	404

404	HODDN65 HODDN92	1352	SEAP in OE-33 Production of IL-6	entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).  IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced lgE production and increases lgA production (IgA plays a role in mucosal immunity).  IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases.  Assays for immunomodulatory	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
-		-		variety of cens where the	Related Disorders, and/or
				expression level is strongly	"Cardiovascular Disorders").

and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and	immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cell-	mediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include inflammatory disorders. Additional highly preferred indications include asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative"
regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to	assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for	immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-

indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain liver and	urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia,	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred
"Lymphocytes: a practical approach" Chapter 6:138-160 a (2000); and Verhasselt et al., J p Immunol 158:2919-2925 [1997), the contents of each of which are herein incorporated ply reference in its entirety of approach and the contents of each of ply reference in its entirety of the contents of each of plants.	may ng n or	when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.  Is g g g in in s s h h
T ap T T T T T T T T T T T T T T T T T T	H. de te as be the other te as an H. de te as an H	who will be a minimum of the control

					indication is infection (e.g., an infectious disease as described below under "Infectious
					Disease").
	HODDN92	1353	Production of	MCP-1 FMAT. Assays for	A highly preferred
405			MCP-1	immunomodulatory proteins	embodiment of the invention
				that are produced by a large	includes a method for
				variety of cells and act to	stimulating (e.g., increasing)
				induce chemotaxis and	MCP-1 production. An
				activation of monocytes and T	alternative highly preferred
				cells are well known in the art	embodiment of the invention
				and may be used or routinely	includes a method for
				modified to assess the ability	<u>.</u>
				of polypeptides of the	MCP-1 production. A highly
				invention (including antibodies	is
				and agonists or antagonists of	infection (e.g., an infectious
				the invention) to mediate	disease as described below
				immunomodulation, induce	under "Infectious Disease").
				chemotaxis, and modulate	Additional highly preferred
				immune cell activation.	indications include
				Exemplary assays that test for	inflammation and
				immunomodulatory proteins	inflammatory disorders.
				evaluate the production of cell	Preferred indications include
				surface markers, such as	blood disorders (e.g., as
				monocyte chemoattractant	described below under
				protein (MCP), and the	"Immune Activity", "Blood-
				activation of monocytes and T	Related Disorders", and/or
				cells. Such assays that may be	"Cardiovascular Disorders").
				used or routinely modified to	Highly preferred indications
				test immunomodulatory and	include autoimmune diseases
				diffferentiation activity of	(e.g., rheumatoid arthritis,

		polypeptides of the invention	systemic lupus erythematosis,
		(including antibodies and	multiple sclerosis and/or as
		agonists or antagonists of the	described below) and
		invention) include assays	immunodeficiencies (e.g., as
		disclosed in Miraglia et al., J	described below). Preferred
		Biomolecular Screening 4:193-	indications also include
		204(1999); Rowland et al.,	anemia, pancytopenia,
		"Lymphocytes: a practical	leukopenia, thrombocytopenia,
		approach" Chapter 6:138-160	Hodgkin's disease, acute
		(2000); Satthaporn and	lymphocytic anemia (ALL),
		Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
		45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
		Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
		158:2919-2925 (1997), the	disease, inflammatory bowel
		contents of each of which are	disease, sepsis, neutropenia,
		herein incorporated by	neutrophilia, psoriasis,
		reference in its entirety.	suppression of immune
		Human dendritic cells that may	reactions to transplanted
		be used according to these	organs and tissues,
		assays may be isolated using	hemophilia, hypercoagulation,
		techniques disclosed herein or	diabetes mellitus, endocarditis,
		otherwise known in the art.	meningitis (bacterial and
		Human dendritic cells are	viral), Lyme Disease, asthma,
		antigen presenting cells in	and allergy Preferred
		suspension culture, which,	indications also include
		when activated by antigen	neoplastic diseases (e.g.,
-		and/or cytokines, initiate and	leukemia, lymphoma, and/or as
	<u>, , , , , , , , , , , , , , , , , , , </u>	upregulate T cell proliferation	described below under
		and functional activities.	"Hyperproliferative
			Disorders"). Highly preferred
			indications include neoplasms

					and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metanlasia and/or dysplasia
405	HODDN92	1353	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications

		macrophage inflammatory	include autoimmune diseases
 		protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
 ·		the activation of	systemic lupus erythematosis,
 		monocytes/macrophages and T	multiple sclerosis and/or as
		cells. Such assays that may be	described below) and
 		used or routinely modified to	immunodeficiencies (e.g., as
 		test immunomodulatory and	described below). Additional
		chemotaxis activity of	highly preferred indications
 		polypeptides of the invention	include inflammation and
 		(including antibodies and	inflammatory disorders.
		agonists or antagonists of the	Preferred indications also
 		invention) include assays	include anemia, pancytopenia,
 		disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,
		Biomolecular Screening 4:193-	Hodgkin's disease, acute
 		204(1999); Rowland et al.,	lymphocytic anemia (ALL),
 	 W.	"Lymphocytes: a practical	plasmacytomas, multiple
 		approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,
 		(2000); Satthaporn and	arthritis, AIDS, granulomatous
		Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
		45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
		al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
 		29 (2000); Verhasselt et al., J	suppression of immune
		Immunol 158:2919-2925	reactions to transplanted
 		(1997); and Nardelli et al., J	organs and tissues, hemophilia,
 		Leukoc Biol 65:822-828	hypercoagulation, diabetes
 		(1999), the contents of each of	mellitus, endocarditis,
 		which are herein incorporated	meningitis, Lyme Disease,
		by reference in its entirety.	asthma, and allergy.
		Human dendritic cells that may	Preferred indications also
		be used according to these	include neoplastic diseases
		assays may be isolated using	(e.g., leukemia, lymphoma,

				techniques disclosed herein or	and/or as described below
				otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
				antigen presenting cells in	indications include neoplasms
				suspension culture, which,	and cancers, such as, leukemia,
				when activated by antigen	lymphoma, prostate, breast,
				and/or cytokines, initiate and	lung, colon, pancreatic,
				upregulate T cell proliferation	esophageal, stomach, brain,
				and functional activities.	liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
		_			disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
i					metaplasia, and/or dysplasia.
	HODDN92	1353	Regulation of	Assays for the regulation of	A highly preferred
405			transcription	transcription through the FAS	indication is diabetes mellitus.
			through the FAS	promoter element are well-	An additional highly preferred
			promoter element	known in the art and may be	indication is a complication
			in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
				assess the ability of	diabetic retinopathy, diabetic
				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
				agonists or antagonists of the	nephropathy and/or other
				invention) to activate the FAS	diseases and disorders as
				promoter element in a reporter	described in the "Renal
				construct and to regulate	Disorders" section below),
				transcription of FAS, a key	diabetic neuropathy, nerve
				enzyme for lipogenesis. FAS	disease and nerve damage
				promoter is regulated by many	(e.g., due to diabetic
				transcription factors including	neuropathy), blood vessel

	SREBP. Insulin increases FAS	blockage, heart disease, stroke
	gene transcription in livers of	impotence (e.g., due to diabetic
	diabetic mice. This	neuropathy or blood vessel
	stimulation of transcription is	blockage), seizures, mental
	also somewhat glucose	confusion, drowsiness,
	dependent. Exemplary assays	nonketotic hyperglycemic-
	that may be used or routinely	hyperosmolar coma,
	modified to test for FAS	cardiovascular disease (e.g.,
	promoter element activity (in	heart disease, atherosclerosis,
	hepatocytes) by polypeptides	microvascular disease,
 	of the invention (including	hypertension, stroke, and other
 	antibodies and agonists or	diseases and disorders as
	antagonists of the invention)	described in the
	include assays disclosed in	"Cardiovascular Disorders"
	Xiong, S., et al., Proc Natl	section below), dyslipidemia,
	Acad Sci U.S.A., 97(8):3948-	endocrine disorders (as
	53 (2000); Roder, K., et al.,	described in the "Endocrine
	Eur J Biochem, 260(3):743-51	Disorders" section below),
	(1999); Oskouian B, et al.,	neuropathy, vision impairment
	Biochem J, 317 (Pt 1):257-65	(e.g., diabetic retinopathy and
	(1996); Berger, et al., Gene	blindness), ulcers and impaired
	66:1-10 (1988); and, Cullen,	wound healing, and infection
	B., et al., Methods in Enzymol.	(e.g., infectious diseases and
	216:362–368 (1992), the	disorders as described in the
	contents of each of which is	"Infectious Diseases" section
	herein incorporated by	below, especially of the
	reference in its entirety.	urinary tract and skin), carpal
	Hepatocytes that may be used	tunnel syndrome and
 	according to these assays, such	Dupuytren's contracture).
	as H4IIE cells, are publicly	An additional highly preferred
	available (e.g., through the	indication is obesity and/or

				ATCC) and/or may be	complications associated with
				routinely generated.	obesity. Additional highly
	_			Exemplary hepatocytes that	preferred indications include
				may be used according to these	weight loss or alternatively,
				assays include rat liver	weight gain. Aditional
<u>.</u>				hepatoma cell line(s) inducible	highly preferred indications are
				with glucocorticoids, insulin,	complications associated with
				or cAMP derivatives.	insulin resistance.
	HODDN92	1353	Activation of	This reporter assay measures	Highly preferred indications
405		-	transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
		_	immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred

												_																	
indications include neoplastic diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes
through the GATA3 response element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Flavell	et al., Cold Spring Harb Symp	Quant Biol 64:563-571 (1999);	Rodriguez-Palmero et al., Eur	J Immunol 29(12):3914-3924	(1999); Zheng and Flavell,	Cell 89(4):587-596 (1997); and	Henderson et al., Mol Cell Biol	14(6):4286-4294 (1994), the	contents of each of which are	herein incorporated by	reference in its entirety. Mast	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human mast cells	that may be used according to
		-																										-	
						- <del>-</del> -																							

				these assays include the HMC- mellitus, endocarditis, 1 cell line, which is an	mellitus, endocarditis, meningitis, and Lyme Disease.
				immature human mast cell line	
		-		established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
HODDN92	192	1353	Activation of	This reporter assay measures	Hiohly preferred indications
	!		transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
				modulate expression of genes	below) and
_				involved in	immunodeficiencies (e.g., as
	)			immunomodulatory functions.	described below). Preferred

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neoplas	emia,	ıma,	ng, color	geal,	er, and	rs and/or	ıder	()	preferr	benign	orders a	litions, s	perplasi	dysplasi	ns incluc	nia,	ocytope	n's dise	anemia	mas,	Burkitt	s, AIDS,	ease,	el diseas	•	ısis,	nune	anted	hemoph
include	.g., leuk	, melano	reast, lur	esophag	rain, liv	ct cancer	selow ur	liferative	). Other	include	ative dis	stic conc	nple, hy	, and/or	ndication	ncytope	, thromk	Hodgki	hocytic	smacyto	yeloma,	, arthriti	tous dise	ory bowe	tropenia	a, psoria	n of imn	transpl	tissues,
indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), plasmacytomas,	multiple myeloma, Burkitt's	lymphoma, arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,
<u>:=</u>	<u>ਰ</u> —		<u>a</u>	d																									0
s for	ugh the	NFAT response element that	outinely	VFAT-	activity	polypeptides of the invention	dies and	onists of	e assays	er et al.,	Cullen an	n Enzyn	92); Hen	Acad Sci	988); De	em Cell	(6661) 9		165(12):7215-7223 (2000);	Hutchinson and McCloskey, J	Biol Chem 270(27):16333-	16338 (1995), and Turner et	8:527-5	nts of ea	which are herein incorporated	s entirety	ay be use	e assays	e (e.g.,
ıry assay	transcription through the	sponse (	sed or re	to test !	element	ides of t	ng antibo	or antag	n) includ	d in Berg	(1998); (	<b>fethods</b> i	-368 (19	oc Natl A	-6346 (19	J Bioch	221-123	mmunol	7215-72	son and I	m 270(2	995), an	Med 18	he conte	e herein	ince in it	ls that m	g to thes	available
Exemplary assays for	transcrip	NFAT re	may be used or routinely	modified to test NFAT-	response element activity of	polypept	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); De Boer	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Ali	et al., J Immunol	165(12):	Hutchins	Biol Che	16338 (1	al., J Exp Med 188:527-537	(1998), the contents of each of	which ar	by reference in its entirety.	Mast cells that may be used	according to these assays are	publicly available (e.g.,
												•												_		_	_		_
						<del></del> .	<u> </u>	<del>7</del>	<del>-</del> _					· the-							<del>.</del> –						-	-	
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				Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of	mellitus, endocarditis, meningitis, and Lyme Disease.
405	НОББИ92	1353	Activation of Endothelial Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment
				tor JNK and p38 kmase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of	of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of

	the invention) include the	endothelial cells. An
	 assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	Exemplary endothelial cells	embodiment of the invention
	that may be used according to	includes a method for
	these assays include human	stimulating angiogenisis. An
	umbilical vein endothelial cells	alternative highly preferred
	(HUVEC), which are	embodiment of the invention
	endothelial cells which line	includes a method for
	venous blood vessels, and are	inhibiting angiogenesis. A
	involved in functions that	highly preferred embodiment
	include, but are not limited to,	of the invention includes a
	angiogenesis, vascular	method for reducing cardiac
	permeability, vascular tone,	hypertrophy. An alternative
	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a

 hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins
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			<i>-</i>							-	<del></del>					<del></del>											_		
				-						-						<del></del> ,													

and/or lymphatics). Highly preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly preferred are indications that	inhibit angiogenesis and/or	cardiovascularization. Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign
											-																
	<u>,</u>											-															

dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud's	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal
										-		-																		
									-																					

		diseases such as acute renal
	 -	failure, and osteoporosis.
		indications include stroke,
		graft rejection, diabetic or
		other retinopathies, thrombotic
	,	and coagulative disorders,
		vascularitis, lymph
		angiogenesis, sexual disorders,
		age-related macular
		degeneration, and treatment
		/prevention of endometriosis
		and related conditions.
		Additional highly preferred
		indications include fibromas,
	-	heart disease, cardiac arrest,
		heart valve disease, and
	 	vascular disease.
		Preferred indications include
		blood disorders (e.g., as
		described below under
		"Immune Activity", "Blood-
		Related Disorders", and/or
		"Cardiovascular Disorders").
		Preferred indications include
-	 •	autoimmune diseases (e.g.,
		rheumatoid arthritis, systemic
•		lupus erythematosis, multiple
	 	sclerosis and/or as described
	 	below) and
		immunodeficiencies (e.g., as

					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
		_			inflammatory diseases, e.g.,
					inflammatory bowel disease
		· · · · · ·	-		and Crohn's disease), and pain
					management.
	800ДДОН	1354	Activation of	Assays for the activation of	A highly preferred
406			transcription	transcription through the CD28	embodiment of the invention
		,.	through CD28	response element are well-	includes a method for
			response element in	known in the art and may be	stimulating T cell proliferation.
			immune cells (such	used or routinely modified to	An alternative highly preferred
			as T-cells).	assess the ability of	embodiment of the invention
				polypeptides of the invention	includes a method for
				(including antibodies and	inhibiting T cell proliferation.
				agonists or antagonists of the	A highly preferred
				invention) to stimulate IL-2	embodiment of the invention
				expression in T cells.	includes a method for
				Exemplary assays for	activating T cells. An
				transcription through the CD28	alternative highly preferred
				response element that may be	embodiment of the invention
				used or routinely modified to	includes a method for
				test CD28-response element	inhibiting the activation of
				activity of polypeptides of the	and/or inactivating T cells.
				invention (including antibodies	A highly preferred
				and agonists or antagonists of	embodiment of the invention
				the invention) include assays	includes a method for
				disclosed in Berger et al., Gene	stimulating (e.g., increasing)
				66:1-10 (1998); Cullen and	IL-2 production. An alternative

				_																			_						
highly preferred embodiment of the invention includes a	method for inhibiting (e.g.,	reducing) IL-2 production.	Additional highly preferred	indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Highly preferred	indications include neoplastic	diseases (e.g., melanoma, renal	cell carcinoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma (e.g.,	metastatic melanoma), renal
Malm, Methods in Enzymol 216:362-368 (1992): Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	McGuire and Iacobelli, J	Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	3(1):552-560 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.								
										-		-																	
																						-							

		-			cell carcinoma (e.g., metastatic	tic
			 		renal cell carcinoma),	
			 _		leukemia, lymphoma (e.g., T	
					cell lymphoma), and prostate,	
					breast, lung, colon, pancreatic,	ာ်
-					esophageal, stomach, brain,	
					liver and urinary cancer. Other	er
			 		preferred indications include	
			 		benign dysproliferative	
			 		disorders and pre-neoplastic	
-			 		conditions, such as, for	
					example, hyperplasia,	-
			 		metaplasia, and/or dysplasia.	-
					A highly preferred indication	
					includes infection (e.g.,	
					AIDS, tuberculosis, infections	S
			 		associated with granulomatous	ns -
			<u> </u>		disease, and osteoporosis,	
					and/or as described below	
					under "Infectious Disease"). A	A
	<del></del> -		 		highly preferred indication is	
					AIDS. Additional highly	
	<del></del>		-		preferred indications include	
					suppression of immune	
		-			reactions to transplanted	
-			 		organs and/or tissues, uveitis,	
-					psoriasis, and tropical spastic	
			 		paraparesis. Preferred	
			 		indications include blood	
	<u></u> .			_	disorders (e.g., as described	
					helow under "Immune	

Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Assays A highly preferred embodiment of the invention activated includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious ts of the under "Infectious Disease").
	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate
	Production of MIP1alpha
	1355
	HODDW40
	407

	immunomodulation, modulate	Preferred indications include
	chemotaxis, and modulate T	blood disorders (e.g., as
	cell differentiation. Exemplary	described below under
	assays that test for	"Immune Activity", "Blood-
	immunomodulatory proteins	Related Disorders", and/or
	evaluate the production of	"Cardiovascular Disorders").
	chemokines, such as	Highly preferred indications
	macrophage inflammatory	include autoimmune diseases
	protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
	the activation of	systemic lupus erythematosis,
	monocytes/macrophages and T	multiple sclerosis and/or as
	cells. Such assays that may be	described below) and
	used or routinely modified to	immunodeficiencies (e.g., as
	test immunomodulatory and	described below). Additional
	chemotaxis activity of	highly preferred indications
	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders.
	agonists or antagonists of the	Preferred indications also
	invention) include assays.	include anemia, pancytopenia,
	disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,
	Biomolecular Screening 4:193-	Hodgkin's disease, acute
	204(1999); Rowland et al.,	lymphocytic anemia (ALL),
	"Lymphocytes: a practical	plasmacytomas, multiple
	approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,
	(2000); Satthaporn and	arthritis, AIDS, granulomatous
~	Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
	45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
	al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
	29 (2000); Verhasselt et al., J	suppression of immune
	Immunol 158:2919-2925	reactions to transplanted
	(1997); and Nardelli et al., J	organs and tissues, hemophilia,

				Leukoc Biol 65:822-828	hypercoagulation diahetes
				(1999), the contents of each of	mellitus, endocarditis,
				which are herein incorporated	meningitis, Lyme Disease.
				by reference in its entirety.	asthma, and allergy.
		,		Human dendritic cells that may	Preferred indications also
				be used according to these	include neoplastic diseases
				assays may be isolated using	(e.g., leukemia, lymphoma,
			_	techniques disclosed herein or	and/or as described below
				otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
				antigen presenting cells in	indications include neoplasms
				suspension culture, which,	and cancers, such as, leukemia,
				when activated by antigen	lymphoma, prostate, breast,
				and/or cytokines, initiate and	lung, colon, pancreatic,
				upregulate T cell proliferation	esophageal, stomach, brain,
,				and functional activities.	liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
			-		conditions, such as, for
					example, hyperplasia,
	HODDW40	1355	Glucose Production		metapiasia, and/or dysplasia.
407			in H4IIE		
	HODDW40	1355	SEAP in		
407			HepG2/Squale-		
			synthetase(stimulati		
			(uo		
Ţ	HODDW40	1355	Regulation of	Caspase Apoptosis. Assays for	Preferred embodiments of the
/ 40 /			apoptosis of	caspase apoptosis are well	invention include using
			immune cells (such	known in the art and may be	polypeptides of the invention

(or antibodies, agonists, or	antagonists thereof) in	detection, diagnosis,	prevention, and/or treatment of	asthma, allergy,	hypersensitivity and	inflammation.																								
used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate caspase	protease-mediated apoptosis in	immune cells (such as, for	example, in mast cells). Mast	cells are found in connective	and mucosal tissues throughout	the body, and their activation	via immunoglobulin E -	antigen, promoted by T helper	cell type 2 cytokines, is an	important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);
as mast cells).		-											71	-																
								-																					7	

		A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred
Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.		Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for P13 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of
	SEAP in OE-33	Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway
	1355	1356
	HODDW40	HODEJ32
	407	408

antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival.	embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is stimulated
Exemplary assays for P13 kinase activity that may be used or routinely modified to test P13 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of	An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell proliferation. In a specific embodiment, skeletal muscle
the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of	cell proliferation is inhibited. A preferred embodiment of the invention includes a method for stimulating muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is stimulated. An alternative
which are herein incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC).	highly preferred embodiment of the invention includes a method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is
Exemplary rat myoblast cells that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary	inhibited. Highly preferred indications include disorders of the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as

"Hyperproliferative Disorders"), endocrine disorders (e.g., as described below under "Fndocrine	Disorders"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), blood disorders (e.g., as described	below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood- Related Disorders"), immune disorders (e.g., as described below under "Immune	Activity"), and infection (e.g., as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),
that fuses to form multinucleated myotubes and striated fibers after culture in differentiation modification modified	differentiation media.			

diabetic neuropathy, nerve	disease and nerve damage (e.g.	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infections	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	

esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.	
	Reporter Assay: construct contains regulatory and coding sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein instincorporated by reference in its
	Inhibition of squalene synthetase gene transcription.
	1357
	HODFN71
	409

HODFN71 1357 1L-2 in Human T-  ell 1293T Assays for the activation of transcription through the through sectum response element in (SRE) are well-known in the immune cells (such art and may be used or as T-cells).  Toutinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or autagonists of the invention) to regulate sectum response factors and modulate the expression of genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention) include assays disclosed in Berger et al., Gene (66:1-10 (1998); Henthom 216:362-368 (1992); Henthom					entirety.	
409 HODFN71 1357 Activation of transcription through the through serum response element in (SRE) are well-known in the immune cells (such art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antiagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention include assays disclosed in Braymol 216:362-368 (1992); Henthorn	409	HODFN71	1357	IL-2 in Human T-cell 293T		·
transcription transcription through the through serum response element in immune cells (such at and may be used or sort—outniely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types.  Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn		HODFN71	1357	Activation of	Assays for the activation of	A preferred embodiment of
through serum response element in response element in immune cells (such as T-cells).  the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antiagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol	409			transcription	transcription through the	the invention includes a
immune cells (such art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists of antibodies and agonists of the invention (including antibodies and agonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types.  Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom				through serum	Serum Response Element	method for inhibiting (e.g.,
immune cells (such art and may be used or as T-cells).  routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types.  Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention) include assays disclosed in Barger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn				response element in	(SRE) are well-known in the	reducing) TNF alpha
as T-cells). routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antibodies and agonists or antibodies and agonists or regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn				immune cells (such	art and may be used or	production. An alternative
the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn				as T-cells).	routinely modified to assess	highly preferred embodiment
the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types.  Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn				`	the ability of polypeptides of	of the invention includes a
antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types.  Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn					the invention (including	method for stimulating (e.g.,
antagonists of the invention) to regulate serum response factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types.  Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn					antibodies and agonists or	increasing) TNF alpha
					antagonists of the invention) to	production. Preferred
factors and modulate the expression of genes involved in growth and upregulate the function of growth-related genes in many cell types.  Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn			-		regulate serum response	indications include blood
expression of genes involved in growth and upregulate the function of growth-related genes in many cell types.  Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn					factors and modulate the	disorders (e.g., as described
in growth and upregulate the function of growth-related genes in many cell types.  Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn					expression of genes involved	below under "Immune
function of growth-related genes in many cell types.  Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn					in growth and upregulate the	Activity", "Blood-Related
n fe ss					function of growth-related	Disorders", and/or
n se s					genes in many cell types.	"Cardiovascular Disorders"),
s o n					Exemplary assays for	Highly preferred indications
n e s	· · · ·				transcription through the SRE	include autoimmune diseases
					that may be used or routinely	(e.g., rheumatoid arthritis,
	10 1070				modified to test SRE activity	systemic lupus erythematosis,
	·		-		of the polypeptides of the	Crohn"s disease, multiple
			· ·		invention (including antibodies	sclerosis and/or as described
- e					and agonists or antagonists of	below), immunodeficiencies
ne m					the invention) include assays	(e.g., as described below),
u					disclosed in Berger et al., Gene	boosting a T cell-mediated
LI (					66:1-10 (1998); Cullen and	immune response, and
					Malm, Methods in Enzymol	suppressing a T cell-mediated
					216:362-368 (1992); Henthorn	immune response. Additional

	53(9):3862- inflammatory disorders, and Black et al., treating joint damage in			pa	entirety. Highly preferred indications		these assays (e.g., leukemia, lymphoma,	ble (e.g., and/or as described below	)). under "Hyperproliferative	T cells that   Disorders"). Additionally,	ding to these   highly preferred indications	JURKAT include neoplasms and	a suspension   cancers, such as, leukemia,		a stimulated.   (e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	
et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-3873 (1994); and Black et al	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety.	Human T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC)	Exemplary human T cells that	may be used according to these	assays include the JURKAT	cell line, which is a suspension	culture of leukemia cells that	produce IL-2 when stimulated.							-						_
					-																							_

				Hodakin's disease acute
				Troughting discuss, addition
				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
		•		disease, inflammatory bowel
				disease, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, Lyme Disease,
				cardiac reperfusion injury, and
				asthma and allergy. An
				additional preferred indication
				is infection (e.g., an infectious
-				disease as described below
				under "Infectious Disease").
HODFN71	1357	SEAP in		
		Molt4/SRE		
HODFN71	1357	Activation of	Assays for the activation of	Highly preferred indications
	77.	transcription	transcription through the	include blood disorders (e.g.,
	,	through NFAT	Nuclear Factor of Activated T	as described below under
		response element in	cells (NFAT) response element	"Immune Activity", "Blood-
		immune cells (such	are well-known in the art and	Related Disorders", and/or
		as natural killer	may be used or routinely	"Cardiovascular Disorders").
-		cells).	modified to assess the ability	Highly preferred indications
			of polypeptides of the	include autoimmune diseases
			ntibodies	(e.g., rheumatoid arthritis,

and agonists or antagonists of	systemic lupus erythematosis,
the invention) to regulate	multiple sclerosis and/or as
NFAT transcription factors and	described below),
modulate expression of genes	immunodeficiencies (e.g., as
involved in	described below), boosting a T
immunomodulatory functions.	cell-mediated immune
Exemplary assays for	response, and suppressing a T
transcription through the	cell-mediated immune
NFAT response element that	response. Additional highly
may be used or routinely	preferred indications include
modified to test NFAT-	inflammation and
response element activity of	inflammatory disorders. An
polypeptides of the invention	additional highly preferred
(including antibodies and	indication is infection (e.g., an
agonists or antagonists of the	infectious disease as described
invention) include assays	below under "Infectious
disclosed in Berger et al., Gene	Disease"). Preferred
66:1-10 (1998); Cullen and	indications include neoplastic
Malm, Methods in Enzymol	diseases (e.g., leukemia,
216:362-368 (1992); Henthorn	lymphoma, and/or as described
et al., Proc Natl Acad Sci USA	below under
 85:6342-6346 (1988);	"Hyperproliferative
Aramburu et al., J Exp Med	Disorders"). Preferred
182(3):801-810 (1995); De	indications include neoplasms
Boer et al., Int J Biochem Cell	and cancers, such as, for
Biol 31(10):1221-1236 (1999);	example, leukemia, lymphoma,
Fraser et al., Eur J Immunol	and prostate, breast, lung,
29(3):838-844 (1999); and	colon, pancreatic, esophageal,
Yeseen et al., J Biol Chem	stomach, brain, liver and
268(19):14285-14293 (1993),	urinary cancer. Other preferred
the contents of each of which	indications include benign

			are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues,
				hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HODFN71	1357	Activation of transcription through serum response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g.,

		antagonists of the invention) to	production. Preferred
		regulate serum response	indications include blood
		factors and modulate the	disorders (e.g., as described
		expression of genes involved	below under "Immune
		in growth and upregulate the	Activity", "Blood-Related
		function of growth-related	Disorders", and/or
		genes in many cell types.	"Cardiovascular Disorders"),
		Exemplary assays for	Highly preferred indications
	-	transcription through the SRE	include autoimmune diseases
		that may be used or routinely	(e.g., rheumatoid arthritis,
	-	modified to test SRE activity	systemic lupus erythematosis,
		of the polypeptides of the	Crohn"s disease, multiple
		invention (including antibodies	sclerosis and/or as described
	-	and agonists or antagonists of	below), immunodeficiencies
,		the invention) include assays	(e.g., as described below),
		disclosed in Berger et al., Gene	boosting a T cell-mediated
		66:1-10 (1998); Cullen and	immune response, and
		Malm, Methods in Enzymol	suppressing a T cell-mediated
		216:362-368 (1992); Henthorn	immune response. Additional
		et al., Proc Natl Acad Sci USA	highly preferred indications
		85:6342-6346 (1988); Benson	include inflammation and
		et al., J Immunol 153(9):3862-	inflammatory disorders, and
		3873 (1994); and Black et al.,	treating joint damage in
		Virus Genes 12(2):105-117	patients with rheumatoid
		(1997), the content of each of	arthritis. An additional highly
		which are herein incorporated	preferred indication is sepsis.
		by reference in its entirety. T	Highly preferred indications
		cells that may be used	include neoplastic diseases
		according to these assays are	(e.g., leukemia, lymphoma,
		publicly available (e.g.,	and/or as described below
		through the ATCC).	under "Hyperproliferative

lay be   Disorders"). Additionally,	ssays   highly preferred indications	ine, include neoplasms and	killer   cancers, such as, for example,	ıd leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organe and fiscuse hemonhilia
Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.																									
									_																					

hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		A highly preferred embodiment of the invention	includes a method for	stimulating T cell proliferation.	An alternative highly preferred	embodiment of the invention	includes a method for	inhibiting T cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	activating T cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting the activation of	and/or inactivating T cells.	A highly preferred	embodiment of the invention	includes a method for
	·	Assays for the activation of	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to stimulate IL-2	expression in T cells.	Exemplary assays for	transcription through the CD28	response element that may be	used or routinely modified to	test CD28-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays
	SEAP in NK16/STAT6	Activation of	through CD28	response element in	immune cells (such	as T-cells).	`													
	1357	1357																		
	HODFN71	HODFN71																		
	409		409																**	

disclosed in Berger et al., Gene 8 timulating (e.g., increasing)  66.1-10 (1998). Culler and  11-2 production. An alternative Mahn, Methods in Enzymol et al., Prov Natl Acad Sci USA et al., Prov Natl Acad Sci USA et al., Brox Natl Acad Sci USA McGuire and lacobelli, J Immunol 159(3):1317, indications include Immunol 159(3):1319, indications include Immunol 159(3):1319, indications include Immunol 159(3):1319, indications include Indemnation and Inflammation and
disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McCuire and lacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):522-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC).  Exemplary human T Cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.

					disorders (e.g., as described
-					below under "Immune
					Activity", "Blood-Related
					Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications also
					include anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
				v	plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HODFN71	1357	Activation of	Assays for the activation of	Highly preferred indications
409			transcription	transcription through the	include inflammation and
-			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,
			as T-cells).	to assess the ability of	as described below under
				polypeptides of the invention	"Immune Activity", "Blood-
				(including antibodies and	Related Disorders", and/or
				agonists or antagonists of the	"Cardiovascular Disorders").
				invention) to regulate NFKB	Highly preferred indications
				transcription factors and	include autoimmune diseases

				line, which is a suspension	metaplasia, and/or dysplasia.
				culture of IL-2 and IL-4	Preferred indications also
				responsive T cells.	include anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HODGE68	1358	Activation of	Assays for the activation of	A preferred embodiment of
410			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	highly preferred embodiment
				the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described

expression of genes involved	below under "Immune
in growth and upregulate the	Activity", "Blood-Related
function of growth-related	Disorders", and/or
genes in many cell types.	"Cardiovascular Disorders"),
Exemplary assays for	Highly preferred indications
transcription through the SRE	
that may be used or routinely	(e.g., rheumatoid arthritis,
modified to test SRE activity	systemic lupus erythematosis,
of the polypeptides of the	Crohn"s disease, multiple
invention (including antibodies	es   sclerosis and/or as described
and agonists or antagonists of	below), immunodeficiencies
the invention) include assays	(e.g., as described below),
disclosed in Berger et al., Gene	le   boosting a T cell-mediated
66:1-10 (1998); Cullen and	immune response, and
Malm, Methods in Enzymol	suppressing a T cell-mediated
216:362-368 (1992); Henthorn	
et al., Proc Natl Acad Sci USA	A   highly preferred indications
85:6342-6346 (1988); Benson	i include inflammation and
et al., J Immunol 153(9):3862-	
3873 (1994); and Black et al.,	
Virus Genes 12(2):105-117	patients with rheumatoid
(1997), the content of each of	
which are herein incorporated	
by reference in its entirety.	Highly preferred indications
Human T cells that may be	
used according to these assays	s (e.g., leukemia, lymphoma,
are publicly available (e.g.,	and/or as described below
through the ATCC).	under "Hyperproliferative
Exemplary human T cells that	t   Disorders"). Additionally,
may be used according to these	se   highly preferred indications
assays include the JURKAT	include neoplasms and